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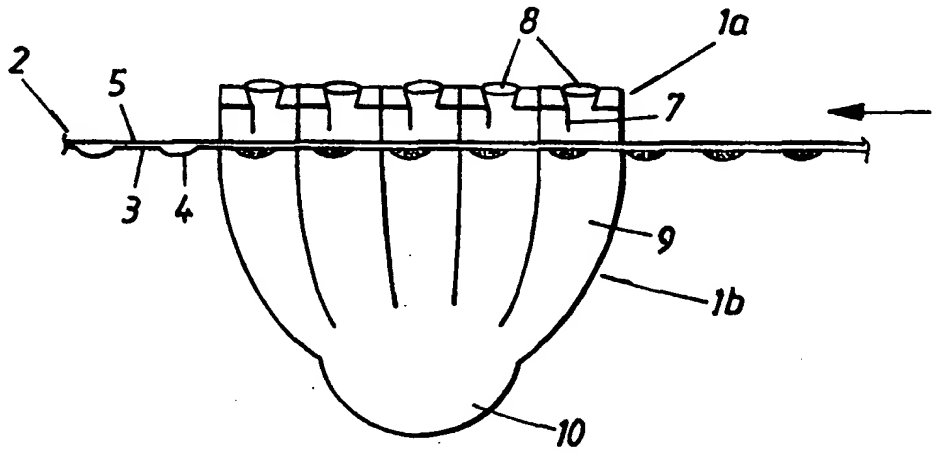


(57) Abstract

A dry powder inhaler, a blister pack and a method of dispensing powder from a blister pack, the blister pack comprising a plurality of blisters, each containing less than a clinical effective dose required of said powder according to the particular one or more substances contained in the powder, the inhaler comprising an inhalation path and dosing means for opening the blisters and releasing the powder into the inhalation path for inhalation by the user, the dosing means comprising opening means suitable for simultaneously opening a predetermined plurality of the blisters such that, for each use of the inhaler, the actual dose administered is determined by the number of blisters which are opened by the opening means, the method comprising opening blisters and releasing powder into a delivery channel, the number of blisters being opened being predetermined according to the desired dose of powder.

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# POWDER INHALER

The present invention relates to a powder inhaler, a blister pack and a method of dispensing powder. More particularly, it relates to a means and method by which a patient may inhale a variable dose of medicament.

It is known that powder containing a medicament may be inhaled for the treatment of certain conditions, such as asthma. Various systems have been proposed for storing and administering the powder.

US 5469843 discloses a system in which a tape is coated with the powder and a sprung hammer strikes the back of the tape to release the powder. W0 94/12230 discloses a device in which an elongate blister pack is successively advanced through the device and in which means are provided for opening a blister and releasing a dose of powder. EP-A-0237507 discloses a device having a bulk powder reservoir from which doses of powder are successively transferred into an inhalation channel.

These various systems all have their own particular advantages and disadvantages, but these will not be considered here.

A disadvantage in common with all of these previous systems is that, within each type of system, it is necessary to provide a wide selection of different inhalers catering for users with different needs and for medicaments requiring different doses.

According to the present invention, there is provided a dry powder inhaler for use with a blister pack having a plurality of blisters, each blister containing a predetermined quantity of powder, the inhaler comprising:

an inhalation path; and

dosing means for opening the blisters and releasing the powder into the inhalation path for inhalation by the user; wherein

the dosing means comprises opening means suitable for simultaneously opening a predetermined plurality of said blisters such that, for each use of the inhaler, the actual dose administered is determined by the number of previously unopened blisters which are opened by the opening means.

The dosing means may comprise a control means for controlling the opening means to open a desired number of the blisters. Alternatively, for each use of the inhaler, the opening means may operate to open all of the predetermined plurality of blisters, the blister pack being positioned in the dosing means according to the required dose, such that the actual dose administered is determined by the number of unopened blisters on which the opening means operates.

In conjunction with this inhaler, the present invention also provides a blister pack comprising a plurality of blisters, each containing a predetermined quantity of powder for inhalation wherein each blister contains less than the clinical effective dose of said powder according to the particular one or more substances contained in the powder.

Thus, according to the present invention there is also provided a method of dispensing powder from a blister pack having a plurality of blisters, each blister containing a predetermined quantity of powder, the method comprising:

opening blisters of the blister pack so as to release the powder contained in said blisters into a delivery channel; and

choosing the number of blisters to be opened so as to provide the powder from said number of blisters in the delivery channel at the same time, the number being determined according to the quantity of powder required to be released into the delivery channel.

The present invention gives rise to many advantages.

Previously, for any one particular medicament, it was necessary to produce a selection of blister packs having respective blisters containing different doses. For instance, one blister pack would be produced having blisters containing the powder dose for an adult and another blister pack would be produced having blisters containing the powder dose for children. Clearly, the need to produce different types of blister pack adds to their cost of production. The present invention allows a single type of blister pack to be used for users with different needs. For instance, for the example given above, a child could use a dose of three blisters whereas an adult could use a dose of five blisters.

Similarly, while previous inhalers require a user to inhale two or more separate doses to receive an extra large dose, the present invention allows the dosage to be varied with a single inhalation.

Another advantage is that only one design of inhaler need be constructed to cater for a variety of blister packs respectively containing many different types of medicament. Any variations required in the dosing between the various different types of medicament may be easily accomplished by the inhaler, which will merely open the required number of blisters.

The present invention allows additional flexibility which has not before been contemplated. In particular, the size of a dose can be varied for each inhalation. This is important for some patients, since their need of medicament can vary, for instance according to the time of day, their body activity or their food intake. In this respect, the present invention is particularly useful in conjunction with antidiabetic substances, such as insulin.

Indeed, according to the present invention, there is also provided a blister pack comprising a plurality of blisters, each containing a predetermined quantity of medicament for inhalation wherein the medicament comprises an antidiabetic medicament.

Medicaments suitable for use with the present invention are any which may be delivered by inhalation. Suitable inhalable medicaments may include for example β2-adrenoreceptor agonists for example salbutamol, terbutaline, rimiterol, fenoterol, reproterol, adrenaline, dpirbuterol, isoprenaline, orciprenaline, bitolterol, salmeterol, formoterol, clenbuterol, procaterol, broxaterol, picumeterol, TA-2005, mabuterol and the like, and their pharmacologically acceptable esters and salts; anticholinergic bronchodilators for example ipratropium bromide and the like; glucocorticosteroids for example beclomethasone, fluticasone, budesonide, tipredane, dexamethasone, betamethasone, fluocinolone, triamcinolone acetonide, mometasone, and the like, and their pharmacologically acceptable esters and salts; anti-allergic medicaments for example sodium cromoglycate and nedocromil sodium; expectorants; mucolytics; antihistamines; cyclooxygenase inhibitors; leukotriene synthesis inhibitors; leukotriene antagonists, phospholipase-A2 (PLA2) inhibitors, platelet aggregating factor (PAF) antagonists and prophylactics of asthma; antiarrhythmic medicaments, tranquilisers, cardiac glycosides, hormones, antihypertensive medicaments, antidiabetic-, such as insulin, antiparasitic- and anticancer-medicaments, sedatives and analgesic medicaments, antibiotics, antirheumatic medicaments, immunotherapies, antifungal and antihypotension medicaments, vaccines, antiviral

medicaments, proteins, polypeptides and peptides for example peptide hormones and growth factors, polypeptides vaccines, enzymes, endorphines, lipoproteins and polypeptides involved in the blood coagulation cascade, vitamins and others, for example cell surface receptor blockers, antioxidants, free radical scavengers and organic salts of N,N'-diacetylcystine.

The present invention will be more clearly understood from the following description, given by way of example only, with reference to the accompanying drawings in which:

Figures 1(a) and 1(b) illustrate a blister pack according to the present invention;

Figures 2(a), 2(b) and 2(c) illustrate schematically the operation of a first embodiment of the present invention;

Figures 3(a) and (b) illustrate an inhaler embodying the present invention;

Figures 4(a) and (b) illustrate an inhaler embodying the present invention;

Figures 5(a) and (b) illustrate an inhaler embodying the present invention;

Figure 6 illustrates a cross-section of an inhaler according to a first embodiment of the present invention;

Figure 7 illustrates a cross-section of an inhaler according to a second embodiment of the present invention;

Figure 8 illustrates a variation of the inhaler of Figure 7; and

Figures 9(a) and 9(b) illustrate alternative blister packs.

Inhalers according to the present invention are preferably to be used with any blister pack containing suitable powder, where each blister contains less than a clinical effective dose of the powder according to the particular medicament contained in the powder such that two or more blisters must be opened to obtain a full dose. However, such inhalers can also be used with blister packs having a clinical effective dose in each blister. Of course, the inhalers would not then be able to administer less than that dose.

Figures 1(a) and 1(b) illustrate a blister pack 2 which is provided as a roll 6. The blister pack is formed from a continuous layer 3 with a series of cavities 4 along its length. Each cavity 4 is filled with a suitable powder and then sealed by a sealing layer 5 which covers the surface of the continuous layer 3. Preferably, perforations exist between each blister, allowing used blisters to be torn off.

The blister pack 2 is inserted into an inhaler 1 as illustrated schematically in Figures 2(a), 2(b) and 2(c).

The inhaler 1 has a first part 1a which functions to open the blisters and a second part 1b which guides air and the powder released from the blisters out of a mouthpiece of the inhaler.

Part 1a of the inhaler 1 is provided with a plurality of cutting means 7 and associated air inlets 8. The cutting means 7 may comprise any suitable means for rupturing the sealing layer 5 of the blister pack 2 and, in some embodiments such as those of Figure 2, for rupturing the lower cavity 4 wall also. In particular, curved or straight blades or pin like members may be used.

In use, with the blister pack 2 inserted in the inhaler 1, the part 1a of the inhaler 1 is moved towards the blister pack such that each of the cutting means 7 ruptures a corresponding blister 4. As illustrated in Figures 2(a), (b) and (c), the cutting means perforate not only the sealing layer 5, but also the continuous layer 3 where it forms the cavities 4. In this way, powder contained in the blisters 4 is released into part 1b of the inhaler 1 below or, at least, is sucked through into part 1b during inhalation by the user.

Part 1b of the inhaler 1 has a series of channels 9 corresponding to the cutting means 7 and air inlets 8 of part 1a. The channels 9 extend to a common inhalation channel 10. Thus, after part 1a of the inhaler 1 has been moved so as to rupture the blisters 4, a user may inhale through the inhaler 1 such that air is drawn through the air inlets 8, picks up powder from the ruptured blisters 4 and passes out of the inhaler via the channels 9 and common inhalation channel 10.

As will be seen by reference to Figure 2(b), if the blister pack 2 is only partly advanced under the cutting means 7 of part 1a of the inhaler 1, when the inhaler 1 is operated, some of the cutting means 7 operate on blisters 4 which have already been ruptured and emptied. In this way, the quantity of powder administered in a single use of the inhaler can be varied.

As mentioned before, the illustrations of Figures 2(a) and (b) are merely schematic and a number of variations are possible.

Firstly, the cutting means 7 need not be provided with individual respective inlets 8, but could be fed with air from a common inlet.

Secondly, the inhaler need not be provided with separate channels 9 and powder from the blisters 4 could move directly into a common inhalation channel.

Thirdly, as illustrated in Figure 2(c), the path of the blister pack 2 need not be straight, but could proceed along a curve.

Figures 3(a) and (b) illustrate the basic features of an inhaler such as described above, Figures 3(b) showing a cross-section of the device of Figure 3(a).

The inhaler 1 has a mouthpiece 12, an inlet opening 14 and an opening means 16. The opening means 16 is axially moveable on one end of the inhaler, preferably against the resistance of a spring which is not shown. It includes a plurality of cutting means 7 each for use with a corresponding blister 4. It also includes a plurality of air inlets 8 corresponding to the cutting means 7. The inlet opening 14 may be formed as a plurality of openings, each forming an end of an air inlets 8 or alternatively as a single opening which feeds the air inlets 8.

In use, once the blister pack 2 has been inserted by an appropriate amount the opening means 16 is pushed towards the mouthpiece 12 such that each cutting means 7 cuts through its corresponding blister 4. With the opening means 16 released, the user may then inhale through the mouthpiece 12, drawing air from the air inlets 8 through the blisters 4 so as to pick up powder in the air stream.

Figures 4(a) and (b) illustrate a similar device in which the opening means 16 takes the form of a button on a side face of the inhaler.

As may be seen from the cross-section shown in Figure 4(b), when the button 16 is depressed, the cutting means 7 are directed through the corresponding blisters 4 so as to perforate them. Figure 4(b) is only schematic and a number of preferred features are not illustrated. For instance, it is preferable to seal the button 16 arrangement such that air only enters the inhaler via inlet opening 14. It is also preferable to provide a spring to return the button 16 and cutting means 7 to their original positions.

Another inhaler according to the present invention will now be described with reference to Figures 5(a) and 5(b).

As with the embodiments described above, the inhaler 1 has a mouthpiece 12, an inlet opening 14 and an opening means 16. In use, a blister pack 2 is inserted into the inhaler 1

according to the number of blisters 4 to be used and the opening means 16 is pressed down into the inhaler 1 so as to rupture those blisters. By inhaling through the mouthpiece 12, air is drawn in through inlet 14, picks up powder from the ruptured blisters 4 and is inhaled.

The embodiment of Figures 5(a) and (b) differs from those described above by virtue of the fact that the cutting means 7 only rupture the sealing layer 5 and the air stream is ducted down onto and over the ruptured blisters.

Figure 6 illustrates a cross-section of the embodiment of Figure 5(b) and shows how the opening means 16 can operate to open a plurality of blisters simultaneously, even those which have already been opened. An equivalent arrangement can easily be derived for the embodiment of Figure 4(b).

The operation described so far can be considered as a first embodiment of the present invention. A second embodiment will now be described.

In the second embodiment, rather than the first part 1a of the inhaler 1 operating as a single unit, it is possible for each of the cutting means 7 (possibly together with their corresponding air inlets 8) to be operated independently. In this way, even when the blister pack 2 is advanced entirely under part 1a of the inhaler 1 as illustrated in Figure 2(a), it is still possible to rupture only some of the blisters 4 which are positioned adjacent the cutting means 7.

Preferably, the blisters 4 which are ruptured are those furthest downstream of the blister pack, such that, after a use, the blister pack may be advanced by the number of blisters 4 which were ruptured during that use so as to once again arrive at the arrangement illustrated in Figure 2(a). Preferably, the inhaler 1 is also provided with a mechanism which, after a number of blisters 4 are ruptured, only allows the blister pack 2 to be advanced by that number of blisters 4.

Figure 7 illustrates a variation of the inhaler of Figure 5(b) which relates to the second embodiment. As may be seen, the opening means 16 of Figure 6 is replaced by a plurality of opening means 16. The opening means 16 thus comprises a means for controlling the number of blisters to be opened. In particular, the number of blisters which are opened is determined by the number of opening means 16 which are depressed by the user. An equivalent arrangement may easily be derived for the embodiments of Figures 3(a) and 4(a).

Figure 8 illustrates a more sophisticated variation of the inhaler of Figure 7 in which a single opening means 16 is provided.

The inhaler of Figure 8 comprises an additional control means 18 with a slider which indicates the selected dosage and a control mechanism controlled by the slider. By altering the position of the slider, the control mechanism varies the number of the cutting means 7 which are engaged by the opening means 16. In this way, the user only operates one opening means 16, but ruptures the number of blisters 4 required for the particular dose.

The control mechanism may also include a moveable stop or a ratchet mechanism, such that the blister pack 2 can only be inserted to a particular position or advanced by a certain number of positions.

Clearly, a slider 18 can also be incorporated in the embodiments of Figures 3(a), 4(a) and 5(a) so as to control the stop position or advancement amount of the blister pack 2.

The slider can of course be replaced by any other control, such as a rotatable knob.

The devices described so far have only been described with reference to a blister pack 2 which is manually inserted/advanced. However, preferably, when the blister pack 2 is provided as a roll 6 such as illustrated in Figures 1(a) and (b), it is installed into the inhaler as a roll and automatically unwound and advanced through the inhaler. The used length of the blister pack 2 can then either exit the inhaler or be wound inside another portion of the inhaler. In the case of first embodiments such as described with reference to Figures 3 to 6, the blister pack 2 should be advanced under the cutting means so as to provide only as many unopened blisters 4 under the cutting means 7 as required. According to this embodiment, the blister pack 2 may be advanced immediately after the inhaler is used or immediately before its next use. It is advantageous for the blister pack 2 to be advanced immediately before each use, because the number of used blisters which are advanced out of the inhaler corresponds to and gives a visual indication of how many blisters are about to be used. Indeed, if the user leaves those used blisters in place, upon using the inhaler again, there is an indication of how many blisters were used previously. This is particularly advantageous when the user has to take different doses alternately. For instance, to obtain an average dose corresponding to 3½ blisters, a user can alternately use 3 and 4 blisters.

In the case of second embodiments such as described with reference to Figure 7, the blister pack 2 should be advanced by the number of blisters 4 previously used. This can easily be achieved by a mechanical ratchet arrangement, with the dosage being set by the user. Alternatively, a more complex electronic arrangement might be provided with motorised advance of the blister pack and detectors to determine which blisters 4 have been already used.

Where the blister pack is advanced out of the inhaler 1, a cutter, such as a blade may be provided at the exit to facilitate used blisters being removed.

Where a blister pack 2 is to be manually inserted, it may be provided as a straight elongate pack. For first embodiments, the blister pack would be inserted merely as far as necessary, whereas, for second embodiments, it would be fully inserted. According to this arrangement, it is possible to provide an inhaler having only an inlet portion whereby, after each use, the user tears off unused blisters from the end of the blister pack, for instance by use of the previously mentioned perforations. For embodiments of the first type, a moveable stop may then be provided to ensure that the blister pack is not inserted further than necessary.

It should be noted that inhalers embodying the present invention are not limited to use with elongate blister packs as illustrated in Figures 1(a) and (b). Any other layout of blisters may also be used.

Figure 9(a) illustrates a blister pack in which blisters are arranged circularly on a disk. With this blister pack, the amount by which the disk is rotated between uses will vary according to the number of blisters ruptured.

Figure 9(b) illustrates a blister pack with blisters arranged across the width of the blister pack as well as along its length. With this blister pack, it is possible that the blister pack is advanced by one row of blisters upon each use, with the dosage administered being controlled according to the number of blisters ruptured across the width of the blister pack.

It is also possible to construct a device which simultaneously accepts two or more blister packs respectively containing different amounts of medicament. In its most straight forward form, the device receives two or more blister pack strips of the type illustrated in Figure 1 and guides them to two parallel sets of cutting means 7 as illustrated in Figures 6

and 7. The user can then individually advance each respective blister pack strip according to the dose required. In particular, when one blister pack strip includes smaller amounts of the medicament than the other strip(s) greater variability may be provided for the administered dose. One blister pack will provide coarse variability and the other blister pack fine variability. Preferably, the device includes a mechanism such that a single operation of the user ruptures blisters of all the strips.

Finally, some consideration should be given to the amount of powder stored in each blister of a blister pack embodying the present invention.

In practice, blister packs are produced having blisters which each contain a clinical effective dose of a particular medicament for any application.

The following medicaments could be administered with the following ranges:

| Compound | Dose range |
|---|---|
| Budesonide | 50μg - 1600μg |
| Terbutaline | 125μg - 12μg |
| Formoterol | 3μg - 48μg |
| Salbutamol | 50μg - 6-700μg |
| Salmeterol | 50μg - 200μg |
| Fluticason | 50mg - 1000mg |

The quantity of medicament stored in each blister should therefore be appropriate to provide a reasonable cover over at least central portions of these ranges according to the maximum number of blisters to be opened simultaneously, for instance between 2 and 8.

In general, it is proposed that each blister should contain one of 10 - 75%, 20 - 50%, 1/4, 1/3 and 1/2 of the clinical effective dose. It is particularly advantageous to provide fractions of the clinical effective dose, since this makes it easier for a patient to determine how many blisters to dispense.

For medicaments, such as antidiabetic medicaments, where the requirements of a user vary continuously between small doses and relatively large doses, the present invention is

ideal. With an antidiabetic medicament contained in blisters, the dose of that medicament may be varied according to the needs of the patient.

For instance, for insulin, the required dose might vary between 0.1mg (1 unit) and 2.0mg (20 units). Preferably, therefore blisters can be provided containing a suitable quantity of insulin to cover this range or at least a more normal range within it. In this regard, it is proposed to use blisters containing one of 0.05 - 0.15mg, 0.15 - 0.25mg, 0.25 - 0.35mg and 0.35 - 0.45mg (½ - 1½ units, 1½ - 2½ units, 2½ - 3½ units, 3½ - 4½ units). In particular, blisters containing 2 units each would allow a range of 2 to 8 units with only 4 blisters per use.

CLAIMS

1. A dry powder inhaler (1) for use with a blister pack (2) having a plurality of blisters (4), each blister (4) containing a predetermined quantity of powder, the inhaler comprising:

an inhalation path (9); and

dosing means (7) for opening the blisters (4) and releasing the powder into the inhalation path (9) for inhalation by the user; wherein

the dosing means (7) comprises opening means (7) suitable for simultaneously opening a predetermined plurality of said blisters (4) such that, for each use of the inhaler, the actual dose administered is determined by the number of previously unopened blisters (4) which are opened by the opening means (7).

2. An inhaler according to claim 1 wherein the dosing means (7) further comprises a control means (16,18) for controlling the opening means (7) to open a desired number of said previously unopened blisters (4).

3. An inhaler according to claim 2 further comprising:

means for advancing the blister pack (2) into the dosing means (7) by an extent corresponding to the number of previously unopened blisters (4) opened during the last use of the inhaler.

4. An inhaler according to claim 1 wherein, for each use of the inhaler, the opening means (7) operates to open all of said predetermined plurality of blisters, the blister pack (2) being positioned in the dosing means (7) according to the required dose such that the actual dose administered is determined by the number of unopened blisters (4) on which the opening means (7) operates.

5. An inhaler according to claim 4 further comprising:

means for advancing the blister pack (2) into the dosing means (7) by an extent corresponding to the number of blisters required to be opened for the desired dose.

6. An inhaler according to claim 4 for use with an elongate blister pack (2) having blisters (4) arranged along its length wherein the dosing means (7) comprises walls defining an aperture into which an end of the blister pack (2) may be inserted, the number of blisters (4) opened by the dosing means (7) being determined by the extent to which the end of the blister pack (2) is inserted.

7. An inhaler according to any one of claims 1 to 5 comprising:

means for storing the blister pack (2,6) within the inhaler (1).

8. An inhaler according to any one of claims 1 to 5 and 7 for use with an elongate blister pack (2) having blisters (4) arranged along its length.

9. A method of dispensing powder from a blister pack having a plurality of blisters, each blister containing a predetermined quantity of powder, the method comprising:

opening blisters (4) of the blister pack (2) so as to release the powder contained in said blisters into a delivery channel (9,10); and

choosing the number of blisters (4) to be opened so as to provide the powder from said number of blisters (4) in the delivery channel (9,10) at the same time, the number being determined according to the quantity of powder required to be released into the delivery channel (9,10).

10. A method according to claim 9 wherein said step of opening includes:

an operating step (7) capable of opening a blister (4) and being performed simultaneously on a plurality of blisters (4); and

a selection step to select on which of the opened and unopened blisters (4) of the blister pack (2) the operating step should be performed, such that the actual dose dispensed is determined by the number of unopened blisters which are opened.

11. A method according to claim 9 wherein said step of opening includes:
an operating step (7) capable of opening a blister (4); and
a control step (16,18) for controlling the number of blisters (4) on which the operating step is performed.

12. A blister pack (2) comprising a plurality of blisters (4), each containing a predetermined quantity of powder for inhalation wherein each blister contains less than the clinical effective dose of said powder according to the particular one or more substances contained in the powder.

13. A blister pack according to claim 12 wherein each blister (4) contains one of 10 - 75%, 20 - 50%, 1/4, 1/3 and 1/2 of said clinical effective dose required of said powder according to the particular one or more substances contained in the powder.

14. A blister pack (2) comprising a plurality of blisters (4), each containing a predetermined quantity of medicament for inhalation wherein the medicament comprises an antidiabetic medicament.

15. A blister pack (2) according to claim 14 wherein the medicament comprises insulin.

16. A blister pack (2) according to claim 14 or 15 wherein each blister (4) contains less than 1mg of said medicament.

17. A blister pack (2) according to claim 14, 15 or 16 wherein each blister (4) contains one of 0.05 - 0.15mg, 0.15 - 0.25mg, 0.25 - 0.35mg, 0.35 - 0.45mg and 0.45 - 0.55mg of said medicament.

Fig. 1a

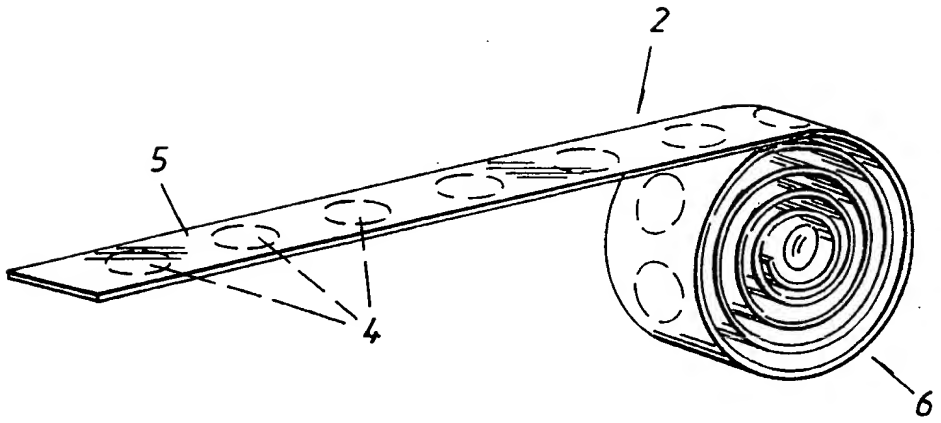



Fig. 1b

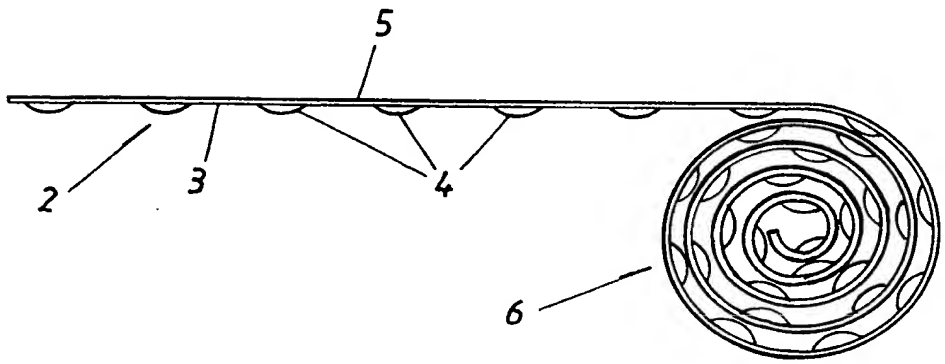


Fig. 2a

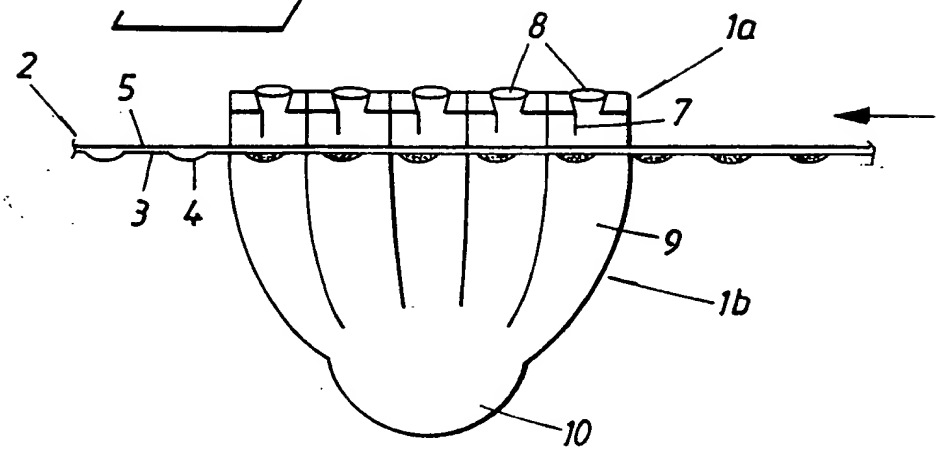



Fig. 2b

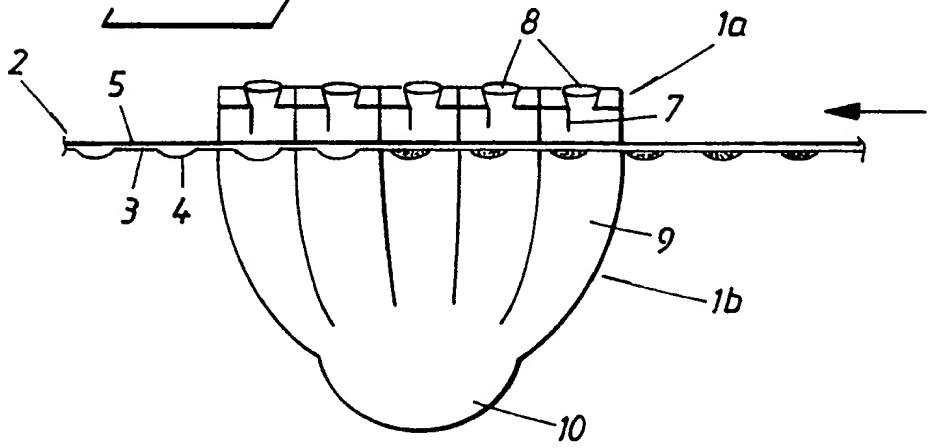



Fig. 2c

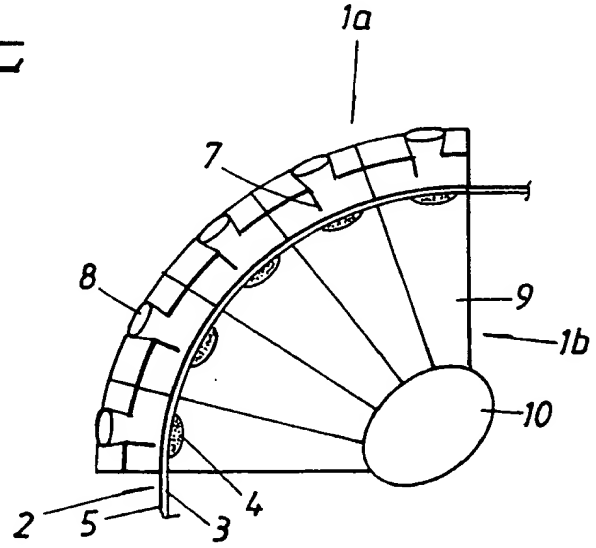


Fig. 3a

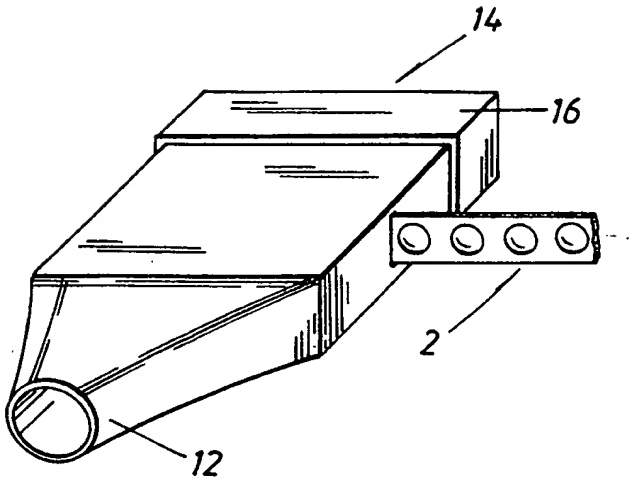



Fig. 3b

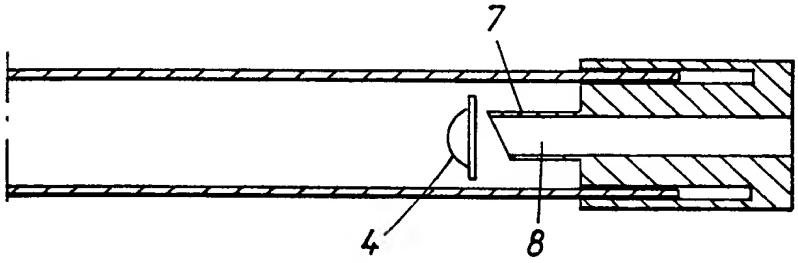



Fig. 4a

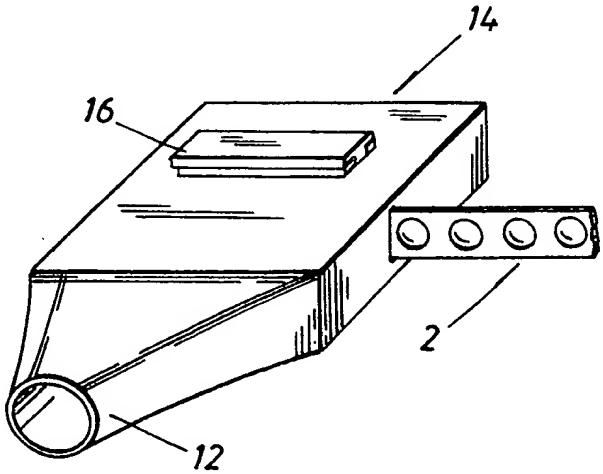


Fig. 4b

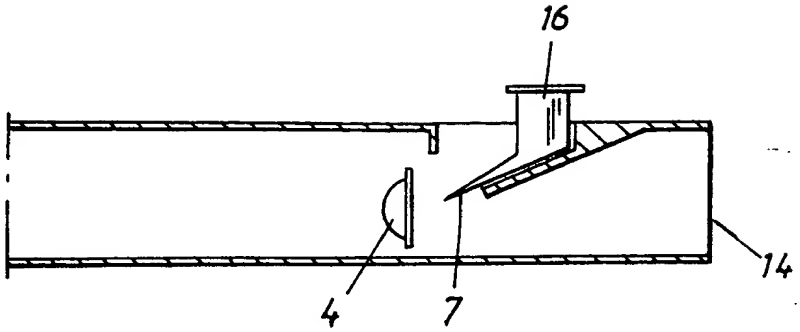



Fig. 5a

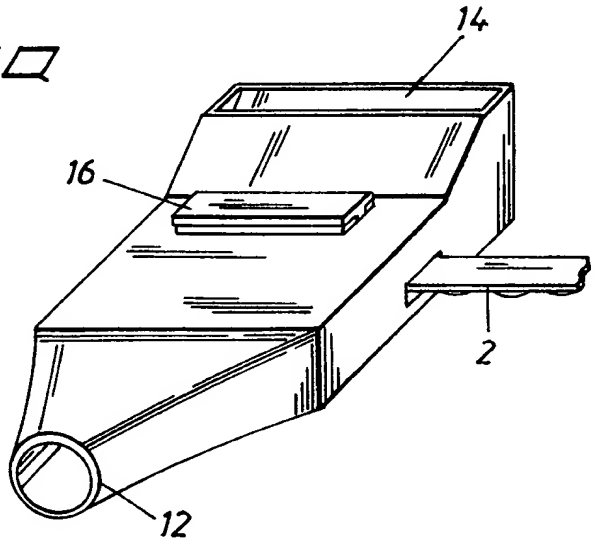



Fig. 5b

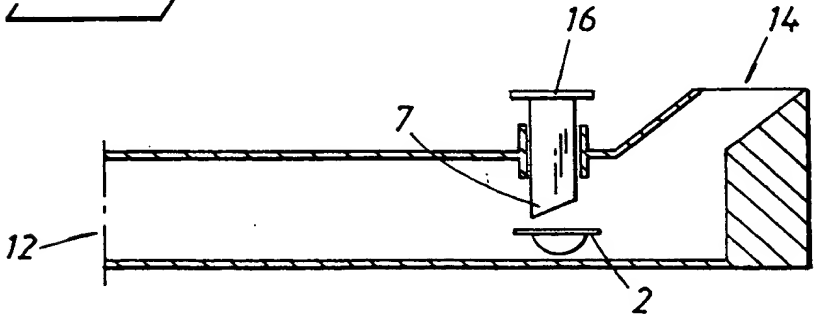


Fig. 6

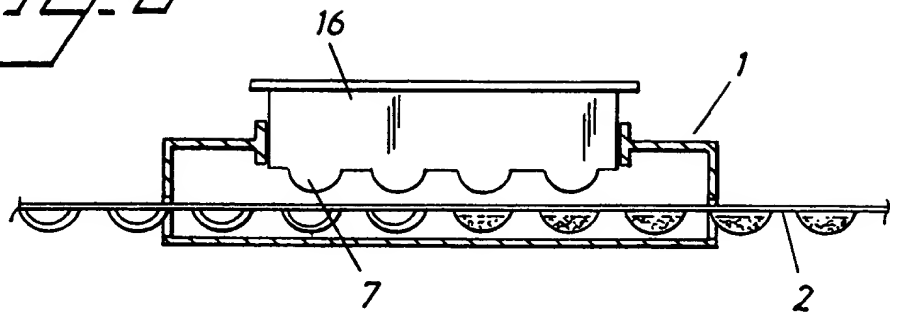



Fig. 7

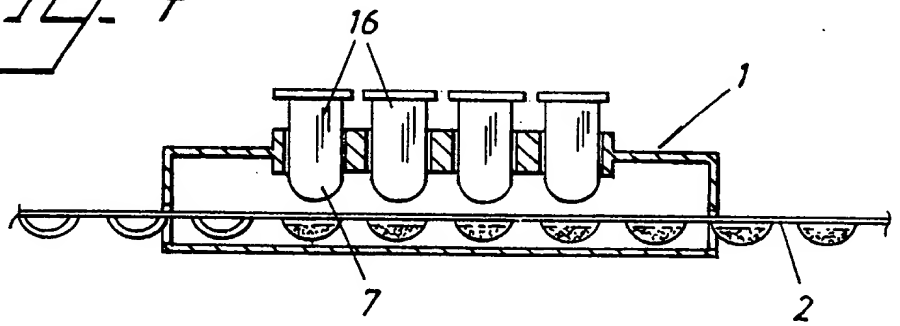



Fig. 8

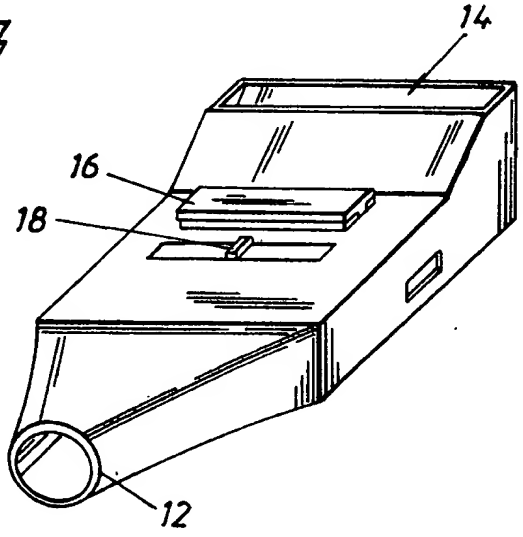


Fig. 9a

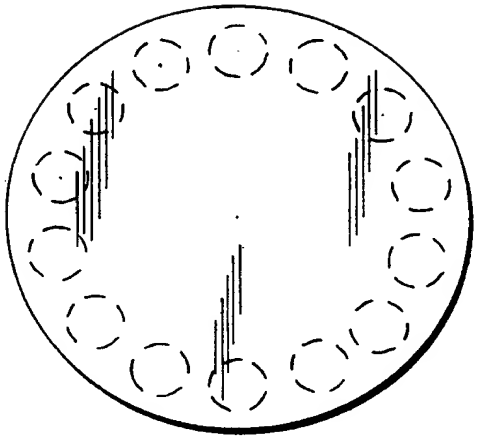
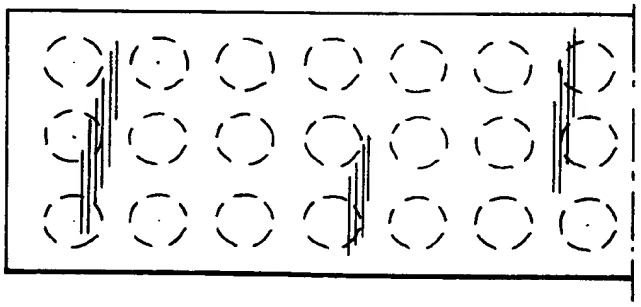


Fig. 9b



# INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 98/00132

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: A61M 15/00, A61K 38/28
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| A | DE 19523516 C1 (ASTA MEDICA AG), 31 October 1996 (31.10.96), column 7, line 38 - column 8, line 16, figure 5 -- | 1-11 |
| A | EP 0469814 A1 (LILLY INDUSTRIES LIMITED), 5 February 1992 (05.02.92), column 3, line 30 - column 4, line 34, figure 1 -- | 1-11 |
| A | US 5415162 A (R.A. CASPER ET AL), 16 May 1995 (16.05.95), figure 1, abstract -- | 1-11 |
| X | US 5544646 A (L.J. LLOYD ET AL.), 13 August 1996 (13.08.96), column 17, line 19 - line 60, figure 2 -- | 14-17 |

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

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| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 16 June 1998 | 24 -06- 1998 |
| Name and mailing address of the ISA/<br>Swedish Patent Office<br>Box 5055, S-102 42 STOCKHOLM<br>Facsimile No. +46 8 666 02 86 | Authorized officer<br>Eva Selin<br>Telephone No. +46 8 782 25 00 |

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 98/00132

**Box I** Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 12-13
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

The claims are not clear and concise, PCT Art. 6, according to the expression "...contains less than the clinical effective dose..." in claim 12.

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II** Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Claims 1-11 relate to a powder inhaler with means for simultaneously opening a plurality of blisters.

Claims 14-17 relate to a blister pack comprising antidiabetic medicament.

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

09/06/98

International application No.
PCT/SE 98/00132

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---|---|---|
| DE 19523516 C1 | 31/10/96 | AU 6004396 A | 05/02/97 |
| | | EP 0835148 A | 15/04/98 |
| | | NO 975924 A | 29/01/98 |
| | | WO 9702061 A | 23/01/97 |
| EP 0469814 A1 | 05/02/92 | CA 2047823 A | 01/02/92 |
| | | JP 5123399 A | 21/05/93 |
| US 5415162 A | 16/05/95 | NONE | |
| US 5544646 A | 13/08/96 | US 5660166 A | 26/08/97 |
| | | US 5718222 A | 17/02/98 |
| | | AU 690561 B | 30/04/98 |
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| | | WO 9427653 A | 08/12/94 |
| | | US 5709202 A | 20/01/98 |

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(30) Priority Data:
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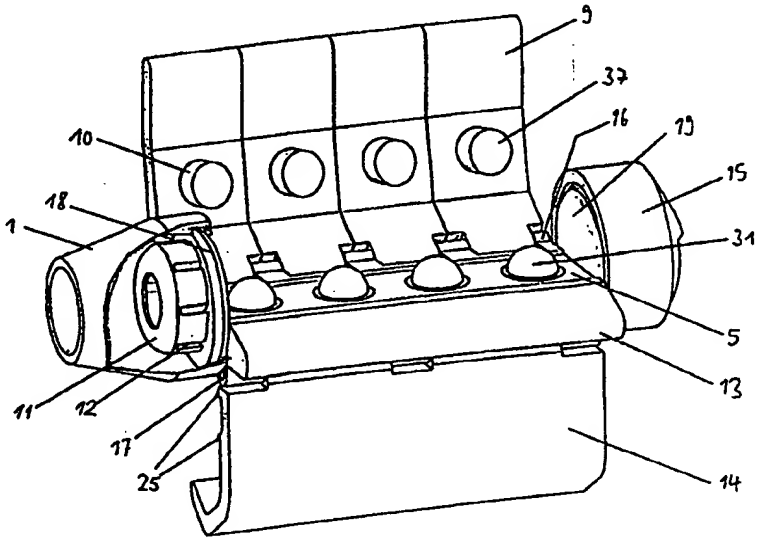
(81) Designated States: AU, BR, BY, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SG, SI, SK, TR, UA, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

**Published**
*With international search report.*

(54) Title: INHALER FOR ADMINISTERING MEDICAMENTS FROM BLISTER PACKS




(57) Abstract

The present invention relates to an inhaler for administering medicaments (38) from blister packs (5), which has a housing with a mouthpiece (1) on one side, an air inlet opening (32) on the opposite side and, between them on the inside, a duct (7) which connects the mouthpiece (1) and the air inlet opening (32), it being possible for at least one blister strip (5) to be inserted into the housing so that the covering foil (35) of the inserted blister strip (5) adjoins the duct (7). The housing has means for pressing out the individual cavities (31) of the blister strip (5), which means contain at least one plunger (10) with a curved plunger surface, which corresponds to the shape of the blister cavities (31), for engagement on the blister cavity.

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# Inhaler for administering medicaments from blister packs

The invention relates to an inhaler for administering medicaments from blister packs, in which the blister cavities are emptied by means of a pressing-out aid.

Inhalers for administering medicaments to patients in a solid form distributed finely in an air flow, so-called powder inhalers, are used nowadays in great numbers and many embodiments in inhalation therapy. They partially replace the previously customary suspension inhalers, in which the aerosol is produced by means of a halogenated hydrocarbon as propellent gas, and whose use is no longer desirable for reasons of environmental protection. Most of the previously known powder inhalers use a device of a technically relatively complex design, with which a patient gives himself inhalable powder portions (doses) by inhalation.

One possibility of predosing medicaments is the packaging of appropriate portions in so-called "blister packs", which are also used, for example, for packaging tablets with the possibility of hygienic individual removal. EP-B-211 595, GB-A-2,129,691 and GB-A-2,142,246 disclose powder inhalers which release the medicament from blister packs in which it is enclosed in a solid, finely distributed form. A disc-shaped blister pack is inserted into the powder inhalers described in EP-B-211,595 and GB-A-2,129,691, the powder portion is released by a plunger when the inhaler is used, and the blister disc is replaced by a new one when it has been completely emptied. GB-A-2,142,246 relates to an inhaler

into which a blister pack comprising a single chamber is inserted and is opened for use with a kind of mandrel.

An inhaler which is easy to handle and is inexpensive is described in the subsequently published DE-A-44 00 084. The inhaler comprises a housing which forms an elongate interior, is sealed off relative to the outside, and has a mouthpiece on a narrow side and an air inlet opening on the opposite side, regions with blister cavities being arranged at least on one main surface of the housing. In one embodiment, the housing comprises an open structure into which one or more strips can be introduced, for example by pushing them or inserting them into a structure which can be pivoted open. In all these embodiments of the inhalers, the user has to press the individual cavities of the blister pack open with his fingers, i.e. exert pressure on the outwardly curved dome so that the thin covering foil tears open and the medicament can drop into the interior of the housing. The disadvantage with these inhalers is that the powder in the blister cavities is mechanically loaded and compressed when the latter are pressed open by the finger, and thus can no longer be finely distributed, or can only be insufficiently distributed, in the inhalation flow.

All these powder inhalers have the disadvantage that they are extremely cumbersome, i.e. the device volume is relatively large in relation to the proportioned dose quantity used. Depending on the volume and number of parts per device, carrying a known powder inhaler can be inconvenient for the patient. Moreover, with the different, often complicated functioning principles, there is the risk that the devices may not be

handled properly, or possibly cannot be handled at all, in an emergency (e.g. in an acute asthma attack) or in the case of little technical understanding on the part of the patient.

The present invention is therefore based on the problem of providing a handy, easy-to-operate powder inhaler for use with blister packs, in which inhaler the compression of the medicament in the blister cavities is avoided during the pressing-out operation so that the medicament can be finely dispersed in the inhalation flow.

This object is achieved by an inhaler for administering medicaments from strip-shaped blister packs, which has a housing with a mouthpiece on one side, an air inlet opening on the opposite side and, between them, a duct and a receiving bearing for a blister strip to be inserted in such a way that the covering foil of the inserted blister strip, which seals the cavities containing the medicament, adjoins the duct, characterized in that the housing has means for pressing out the individual cavities of the blister strip, and these means have at least one plunger with a curved plunger surface which corresponds to the shape of the convex blister cavities.

Preferred embodiments of the invention are described in the subclaims.

The inhaler according to the invention serves to administer medicaments from blister packs. Blister packs are packs which comprise a container film with small, filled depressions or cavities and a covering foil which seals the depressions. In this case, the term "blister pack" is to be understood within the scope of the

present invention in the widest sense for packs of this type, irrespective of the type of container film or its method of manufacture. The container film has such a wall thickness in the region of the cavities that it is possible to press the cavity in from the outside, and the covering foil tears open as a result of the pressing-in. The operation of pressing the cavity in from the outside with simultaneous tearing-open of the covering foil and release of the medicament is described in the following as "pressing-out".

The housing of the inhaler according to the invention preferably has an elongate shape with the mouthpiece on one narrow side and the air inlet opening on the opposite narrow side. The blister strip which is inserted into the housing has a row of cavities arranged one after the other. The inhaler is designed in such a way that it can only ever receive blister strips with a particular number of cavities, the number of cavities depending on the type and dosage of the medicament to be administered. An inhaler which is suitable for many applications is designed for the use of blister strips with four cavities.

A preferred embodiment of the inhaler has a housing which can be pivoted open and comprises at least two housing parts which are pivotably connected to one another via a joint or hinges. The housing can, for example, have a bottom part and an upper part, which parts are pivotably connected to one another, or it can even have an additional central part. In the bottom part or central part of the housing, there is a receiving bearing with a recess for receiving the blister strip. The upper part of the housing may additionally have

inwardly directed webs for pressing the blister strip against the receiving bearing in order to fix the blister strip in the closed inhaler.

The pressing-out means of the inhaler according to the invention have at least one plunger with a curved plunger surface adapted to the shape of the blister cavities. Since the customary blister packs have cavities whose curvature has the shape of a spherical cap from the outside, the curvature of the engaging plunger surface is usually designed to be complementary to a spherical cap. The concave curvature of the engaging plunger surface adapted to the convexly curved shape of the blister cavities prevents the medicament from being compressed inside the cavities when they are pressed out and thus from no longer being able to be dispersed sufficiently in the air flow.

The pressing-out means are advantageously integrated in the housing. In order to open and to empty a blister cavity with the aid of the pressing-out means, the user has to press parts of the pressing-out means or the entire pressing-out means with his fingers or whole hand. In this case, the transmission of force to the plunger of the pressing-out means, whose surface engages on the outwardly curved blister cavity, can take place directly or by means of a lever transmission. In the case of means with leverage, these can be designed in the form of a plurality of individual levers, each having a pressing-out plunger, or as one lever with a displaceable, engaging pressing-out plunger.

In a preferred embodiment of the invention, the pressing-out means are integrated in the upper part of the housing and act without a lever transmission.

Particularly advantageous is a constructional design of the pressing-out means with four pressing-out plungers which are mounted in the upper part of the housing by means of grip plates and, when required, are pressed down by the user one after the other in order to empty the blister cavities.

In another preferred embodiment of the invention, the upper part of the housing itself forms the pressing-out means. Particularly advantageous is the design of the upper part of the housing as a single lever with a displaceable, engaging pressing-out plunger. As an alternative thereto, the upper part of the housing can also be formed from a plurality of single levers which are pressed down one after the other for use.

The pressure due to the plunger surface on the cavity causes the thin covering foil of the blister pack to tear open and the medicament either still to remain in the cavity due to adherence forces or to drop directly into the powder duct of the housing.

During inhalation by sucking on the mouthpiece of the inhaler, the user generates a slight negative pressure in the air duct, which causes the medicament still remaining in the cavity to be conveyed into the duct and air to enter the duct through the air inlet opening. Moreover, since the air flow in the duct generates a partial negative pressure when flowing past the opened cavity (injection effect), the medicament is to a great extent sucked out of the cavity without leaving a residue. The air flow then exits from the inhaler via the mouthpiece, carrying the medicament

along with it, and is inhaled by the user so that the medicament can pass into the lung.

For reasons of favourable air conduction in the air duct, it is advantageous to tear open or sever the covering foil of the blister pack in a defined manner. It is therefore desirable for the part of the covering foil which originally sealed the cavity to project into the interior of the duct after opening as a kind of tag which is attached at only one point, the intention being for the tag to be aligned parallel to the air flow. This is achieved, for example, by using specially designed blister packs. For instance, the individual cavity may be partially surrounded by an annular bead, as a result of which the covering foil is severed, during pressing-out, in the region of the bead and, in the region in which the bead is interrupted, remains connected to the remaining covering foil; or the covering foil is provided with predetermined tearing points. The asymmetrical design of the cavities, for example in a shape which is chamfered on one side, likewise leads to a defined tearing-open of the covering foil.

In order to achieve defined tearing-open of the covering foil when using customary blister packs, the plunger must engage asymmetrically on the blister cavity during the pressing-out operation. This is achieved, for example, by the pressing-out plunger itself having an asymmetrical cross-section, i.e. the edge of the curved plunger surface extends in a plane which, at an angle not equal to 90° relative to the longitudinal axis of the plunger, intersects a perpendicular plane extending in the longitudinal direction of the housing, so that the plunger engages firstly on one side of the outwardly

curved blister cavity when it is pressed down. The covering foil then tears open firstly in this contact region, while it remains connected to the remaining covering foil on the opposite side of the cavity. A likewise asymmetrical engagement of the plunger on the blister cavity is achieved in a symmetrically designed pressing-out plunger if the latter is connected to the housing laterally by means of a lever arm in such a way that the plunger, when it is pressed down by the user, carries out a movement along an arc about the pivot of the housing part, and that the engagement on the blister cavity firstly takes place on one side. The pressing-out plunger of asymmetrical cross-section in the longitudinal direction can also be combined with the lever arrangement. Of course, the blister packs with asymmetrical cavities described above can also be used in an inhaler in which the pressing-out device engages asymmetrically on the blister cavity.

Preferred embodiments of the inhaler according to the invention have a mouthpiece, in whose interior a cyclone chamber with tangential air inlet slots is arranged, into which secondary air can enter through an appropriate duct. When, after opening a blister cavity, the user sucks on the mouthpiece, the medicament passes via the duct to the mouthpiece where, due to the cyclone effect, it is dispersed with tangentially inflowing secondary air and is thus rendered more readily inhalable. This secondary air, sucked in to assist the powder dispersion, preferably amounts to about 75% of the total air flow. This means that about 25% of the total air flow is conducted through the duct. On account of this air flow, the medicament is conveyed from the

cavity through the air duct, through a corresponding opening, perpendicularly onto a deflector and then tangentially through a further opening into the cyclone chamber.

In order to prevent the medicament dropping out through the air inlet opening after a blister cavity has been pressed out, due to the inhaler being held vertically, the space directly behind the opening can be provided with built-in webs which deflect the air path and extend it in the form of a labyrinth. In order furthermore to avoid the medicament being carried out of the inhaler by air being blown into the mouthpiece, the air inlet opening for the powder duct is preferably provided with a non-return valve which opens under a slight negative pressure in the interior of the housing and closes under normal or overpressure in the housing interior. A suitable non-return valve is a diaphragm valve in which a diaphragm is arranged on the inner side of the housing, which diaphragm covers the inlet opening and is placed against the end face, under overpressure in the housing, and closes the inlet opening. Spring-loaded ball valves or other non-return valves can also be used for closing the air inlet opening.

The housing of the inhaler according to the invention can have one or more additional recesses or chambers to receive one or more replacement blister packs.

The inhaler is preferably made of plastic; suitable materials are, for example, thermoplastics, such as polyoxymethylene (polyacetal), polycarbonate, polymethylmethacrylate, polypropylene, polyethylene, polyvinyl chloride and acrylonitrile-butadiene-styrene

copolymer (ABS), singly or in combination. Elastomeric polymers with spring-elastic characteristics are suitable for the design of the webs for fixing the blister strip.

Blister packs made of various materials can be used in the inhaler of the present invention. The material of the container film is preferably a thermoformable polymer, such as polypropylene, polyethylene, polyvinyl chloride, polystyrene, or a metal which can be deep-drawn, such as aluminium, also with a laminated polymer. zOther thermoformable materials customary for blister packs are also suitable. Such shaped parts with depressions produced by thermoforming have an even wall thickness of the container film both over the areas of the depressions and over the other areas. However, an injection-mouldable material or another mouldable material or a material which can be processed by blow-moulding, for example an elastomeric material, can also be used, for example, as material for the container film, and the shaped part with the depressions can correspondingly be produced by injection-moulding or another moulding method or by blow-moulding. In this case, the wall thickness of the container film can be varied optionally in various areas. The covering foil is preferably made of metal, for example aluminium, or aluminium alloys, with a laminated polymer. Other materials, including those which are customary and known for blister packs, can also be used. The covering foil can be connected to the container film in various ways, for example by welding or bonding as is customary. In the inhaler according to the invention, it is also possible to use blister packs in which the individual

cavities are surrounded by an annular bead moulded out of the container film. These blister packs have the advantage of additionally reducing the mechanical loading on the medicament during pressing-out.

A powder inhaler for use with blister packs is provided by the present invention, which inhaler is easy to operate and provides the medicament to the user in a sufficiently dispersed and thus inhalable form.

The invention will be explained with reference to different embodiments illustrated in the following figures.

Figure 1 shows, in a perspective illustration, an inhaler with a pressing-out means designed as a single lever.

Figure 2 shows a cross-section of the inhaler illustrated in Figure 1 with the housing pivoted open and a blister cavity in cross-section.

Figure 3 shows a cross-section of the inhaler illustrated in Figure 1 with the housing pivoted closed and a blister cavity inserted.

Figure 4 shows a cross-section of the inhaler from Figure 1 with a single lever pressed down.

Figure 5 shows, in a perspective illustration, an inhaler with four individual pressing-out levers pivoted open and the bottom part of the housing pivoted down.

Figure 6 shows a cross-section of the inhaler illustrated in Figure 5 with the housing closed and a blister strip inserted.

Figure 7 shows, in a perspective illustration, an inhaler with four central pressing-out aids and the upper part of the housing pivoted open.

Figure 8 shows a longitudinal section of the blister inhaler illustrated in Figure 7 with the housing fitted together and a blister strip inserted.

Figure 9 shows a cross-section of the inhaler illustrated in Figure 8.

Figure 10 shows the inhaler from Figure 9 with a pressing-out plunger pressed down.

All the inhalers illustrated are for the use of blister strips with four successively arranged cavities which are emptied successively by the user and whose content is inhaled.

In the embodiment of the present invention illustrated in Figure 1, the pressing-out device is designed as a single lever 2 which constitutes the upper part 2 of the housing at the same time. The upper part 2 of the housing is connected to the bottom part 3 of the housing by means of a film hinge, the upper part 2 of the housing engaging slightly beyond the bottom part 3 of the housing in the fitted-together state. A mouthpiece 1, shaped essentially like a truncated cone, is attached to the narrow side of the bottom part 3 of the housing. Located in the single lever 2 is a rectangular recess 27 in which the approximately square grip plate 4 of the pressing-out plunger 10 engages (not visible in Figure 1). The grip plate 4 is displaceable in the recess 27, it being possible for the said grip plate to be fixed in an engaging manner in the positions a, b, c or d by means of corresponding notches 28. Prior to the inhaling operation, the displaceable pressing-out plunger 10 must be pushed by means of the grip plate 4 over a blister cavity 31 which has not yet been emptied (not visible in Figure

1), i.e. the pressing-out plunger 10 is positioned with the engaging function at one of the four pressing-out positions a, b, c or d. By pressing down the upper part (single lever) 2 of the housing, the blister cavity 31 located below the pressing-out plunger 10 is pressed out. In this embodiment of the inhaler, the pressing-out of a blister cavity 31 can take place not only with the index finger and thumb, but also with the whole hand, since the single lever 2 provides a broad application surface. In order to prevent slipping-off, it is additionally provided on the surface with longitudinally extending gripping grooves 35. The arcuate recess 36 in the upper part 2 of the housing and the gripping grooves 35 in the bottom part 3 of the housing facilitate the opening of the housing. In the fitted-together state, the housing is held closed by means of a pin 42 which engages in a cutout 41 in the mouthpiece 1 and the bottom part 3 of the housing. The pin 42 is attached to the upper part of the housing or single lever 2 and can be lowered in the cutout 41 when the single lever 2 is pivoted down. In order then to avoid the single lever 2 pivoting up, the mouthpiece 1, which is rotatable, is turned through about 30°. The wall of the mouthpiece 1 slides over the end of the pin 42 in such a way that the opening operation is blocked, but the single lever 2 can nevertheless be pressed downwards to press out a blister cavity 31. To open the housing, the mouthpiece 1 is turned back in the opposite direction so that the part of the cutout 41 on the mouthpiece 1 exposes the pin 42 on the single lever 2, and the single lever 2 can be pivoted upwards.

The interior design of the housing can be seen in the cross-sectional illustrations of Figure 2 to Figure 4. Arranged in the bottom part 3 of the housing is a receiving bearing 29 for the blister strip 5, which receiving bearing comprises two longitudinally extending plates directed upwards in a V-shape. Apart from the longitudinally extending plates which can be seen in the cross-sectional drawings, the receiving bearing 29 also has two corresponding transversely extending plates on the short sides of the housing, such that the inserted blister strip 5 rests with all four sides on the bearing 29. The plates of the bearing 29 are widened slightly in the upper region in order to provide a sufficient resting surface for the blister strip 5; moreover, the plates have, at their widened upper end, an inwardly directed recess 30 of small depth, into which the blister strip 5 is inserted and which prevents the blister strip 5 from slipping inside the bearing 29. The duct 7 extending longitudinally through the housing is located in the lower region between the plates of the bearing 29 arranged in a V-shape. The duct 7 connects the mouthpiece 1, which is only visible in the perspective illustration of Figure 1, to the air inlet opening which is not illustrated in this embodiment. The plates of the bearing 29 enclose, with the walls of the bottom part 3 of the housing, two chambers 34 which extend to the right and left next to the air duct 7 and in which blister strips 5 for later use (so-called "replacement blister strips") can be kept.

The plunger 10 with a concavely curved plunger surface 37 which is connected integrally to the

grip plate 4 can be seen in Figures 2 to 4. The longitudinally slidable connection to the upper part 2 of the housing takes place via the grip plate 4. The part 40 of the upper part of the housing adjoining the film hinge acts as an inner or integrated lever for the plunger 10.

Figure 2 shows the single-lever inhaler with the housing open, i.e. the upper part 2 of the housing is pivoted upwards and the blister strip 5 can thus be placed on the bearing 29. Apart from the plunger 10, there are also two inwardly directed thin webs 6 on the single lever 2 along the long sides of the recess 27 (see Figure 1), the web ends 6a remote from the inner surface of the upper part 2 of the housing being bent for engaging around the receiving bearing 29. There are transverse webs between the end-face ends of the webs 6. The webs 6 and the transverse webs are made of spring-elastic material so that they can be deformed (curve) when the upper part 2 of the housing is pressed down for the engagement of the plunger 10 on a blister cavity 31 and, with the spring force, press the edge of the blister strip into the bearing 29.

Figure 3 shows the inhaler with the housing closed and a blister strip 5 inserted in the first stage of the pressing-out operation. It can be seen how the elastic webs 6 engage on the upper ends of the bearing 29 and the blister strip 5 inserted therein. Since pressure is exerted on the single lever 2 by the user (not illustrated here) from above, the webs 6 are already under stress. The web 6 is designed in such a way that it presses all four sides of the blister strip under stress firmly onto the bearing 29 in order to fix

the blister strip 5 so as to be sealed off with respect to air to a great extent. Since the plunger 10 is connected laterally to the bottom part 3 of the housing by means of an inner lever arm 40, the plunger 10 describes an arc about the pivot of the upper part 2 of the housing when the upper part of the housing is closed and, as a consequence thereof, the engagement of the edge of the curved plunger surface 37 on the outwardly curved blister cavity 31 takes place asymmetrically, i.e. in the first phase of the pressing-out operation firstly only on one side. In the stage of the pressing-out operation illustrated in Figure 3, the upper part 2 of the housing engages slightly over the bottom part 3 of the housing.

Figure 4 illustrates the final phase of the pressing-out operation with a blister cavity 31 which has already been opened and emptied. In comparison with Figure 3, the webs 6 are even more stressed and the upper part 2 of the housing engages further over the bottom part 3 of the housing. The blister cavity 31 was pressed out by means of the plunger 10; the covering foil which previously sealed the blister cavity 31 is still connected to the blister strip 5 only on one side and hangs down as a tag 8, aligned parallel to the air flow, in the interior of the duct 7. The asymmetrical engagement of the plunger 10 on the blister cavity 31 caused the covering foil to tear open firstly on the side on which the curved plunger surface 37 firstly engaged. In Figure 4, the medicament 38 drops from the opened blister cavity 31 straight into the air duct 7, from where it is made accessible to the user by means of the inhalation operation which then follows. The

bold arrow in Figure 4 is intended to show clearly at which point the application of force by the user takes place during the pressing-out operation. The lever transmission means that the effort required for pressing out the blister cavity 31 is to be less by about half than in the case of a direct pressing-out operation. When all four cavities 31 of the blister strip 5 have been emptied, the housing must be opened and a new blister strip 5 inserted.

Figures 5 and 6 likewise show an embodiment of the inhaler in which the pressing-out means act by means of lever arms. However, in this case, there is not just a single lever arm 2 with a displaceable pressing-out plunger 10, but there are four individual pressing-out levers 9, each having a pressing-out plunger 10, which plungers are actuated successively for pressing out the four blister cavities 31. Figure 5 shows the four-lever inhaler with the housing pivoted open. The bottom part 14 of the housing is pivotably connected to the central part 13 of the housing by means of an appropriate hinge 17 which is attached to the long side of the central part 13. The four pressing-out levers 9 are likewise pivotably connected to the central part 13 of the housing via an appropriate hinge 16 which is located on the opposite long side of the said central part 13 of the housing. The upper side of the central part 13 of the housing serves as a bearing for the blister strip and has, in the centre, a rectangular recess 30 for receiving the blister strip 5. Formed in the bottom of the recess 30 are four supply openings 20 which are not visible in Figure 5 and which communicate with the air duct 7 when

the housing is closed. Attached to one narrow side of the central part of the housing is a receiving plate 18 for the mouthpiece 1, and a receiving plate 19 for the end piece 15 is attached to the opposite narrow side. A cyclone chamber 11 with tangential air inlet slots 12 is formed on the receiving plate 18 for the mouthpiece 1. The mouthpiece 1, which comprises a cylindrical section and a section shaped like a truncated cone, is fastened to the receiving plate 18 and, with its cylindrical section, surrounds the cyclone chamber 11. In order to allow the entry of secondary air into the cyclone chamber 11 via the air inlet slots 12, the mouthpiece 1 has a secondary-air duct which is not illustrated here. The end piece 15 with an air inlet opening, not illustrated here, and a diaphragm valve is fastened to the receiving plate 19. The air duct 7 extends on the inner side of the pivotable bottom part 14 of the housing and is sealed off towards the side in an airtight manner only when the housing is closed by means of corresponding beads 25 extending longitudinally along the duct. When the bottom part 14 of the housing is pivoted open, the duct 7 is open and is thus easily accessible for cleaning. When the housing is closed, the duct 7 connects the air inlet opening to the mouthpiece 1 via corresponding openings in the receiving plates 18 and 19.

After the blister strip 5 has been inserted into the central part 13 of the housing, as shown in Figure 5, the housing is pivoted closed, specifically in that firstly the four pressing-out levers 9 which in a certain way form the upper part of the housing are pivoted slightly downwards, but without already

exerting pressure on the blister cavities 31 in the process, and the bottom part 14 of the housing is then pivoted upwards. Figure 6 shows a cross-section of the four-lever inhaler pivoted closed. The end of the bottom part 14 of the housing located opposite the hinge 17 is bent over so that, in the pivoted-closed state, it engages around the pressing-out levers 9 on their lower part, and the housing remains closed by means of this engaged connection. The bottom part 14 of the housing is bent over in such a way and the pressing-out levers 9 are shaped in such a way that the plungers 10 exert slight pressure on the blister cavities 31 when the housing is closed, thus fixing them in the recess 30, but without already pressing the blister cavities 31 out. The blister strip 5 is fixed by the pressing-out levers 9 resting on it in such a way that the strip 5 cannot drop out or be removed in the closed state of the inhaler. The curvature of the bottom part 14 of the housing also means that the bottom part 14 of the housing merely needs to be pivoted upwards to close the housing, thus bringing the pressing-out levers 9 automatically into the position shown in Figure 6. It can easily be seen in Figure 6 how the duct 7 is sealed off laterally by the two longitudinally extending beads 25 which press against the central part 13 of the housing. If the user then wishes to inhale a dose of the medicament 38 enclosed in the blister cavities 31, he must press down one of the four pressing-out levers 9, preferably utilizing the lever transmission at the end remote from the hinge 16, the plunger 10 exerting pressure, by means of its curved plunger surface 37, on the blister cavity 31 and

pressing the latter out. The bold arrow denotes such a preferred point for the application of force on the lever 9 by the user. As can be seen in Figure 6, an asymmetrical engagement on the blister cavity 31 takes place in this embodiment too, due to the arrangement of the plunger 10 on an inner lever arm 40 connected laterally to the central part 13 of the housing, in order to tear open the covering foil 39 at one point in a targeted manner. The medicament then drops through the supply opening 20 into the duct 7 and is inhaled from there. In order to release the next dose of the medicament, a further pressing-out lever must be pressed down. Since the pressing-out levers 9 in this embodiment are considerably narrower than the single lever 2 of the embodiment described above, and since these have to be actuated individually, the pressing-out levers 9 should be pressed down by the user using one finger. Just as in the single-lever design, the effort required in this embodiment for pressing-out the blister cavities 31 is less by about half, due to the lever transmission, than in the case of a direct pressing-out operation. A particular advantage of this embodiment is the easy accessibility of the powder duct 7 and of the supply openings 20 for cleaning purposes when the housing is pivoted open.

Shown as a further embodiment in Figures 7 to 10 is an inhaler with pressing-out means which act directly, i.e. without lever transmission. It can be seen in Figures 7 and 8 that the inhaler comprises an elongate bottom part 3 of the housing with a mouthpiece 1 and an end piece 15 and an upper part of the housing, which is described here as a housing flap 23, with

integrated pressing-out plungers 10. With the housing flap 23 closed, the housing has an essentially tubular shape. The housing flap 23 is connected to the end piece 15 of the bottom part 3 of the housing via a hinge 24. Located in the housing flap 23 is a rectangular recess 22 in which four pressing-out plungers 10 are mounted with their grip plates 4. In the bottom part of the housing 3 there is a likewise rectangular recess 30 as a bearing for the blister strip 5. Arranged in the bottom of the recess 30 are four supply openings 20 which communicate with the powder duct 7 which is not visible in Figure 7. The closed housing flap 23 engages in the recess 30 of the bottom part 3 of the housing and thus fixes the inserted blister strip 5. Located in the end piece 15 is the air inlet opening 32 which is provided with a diaphragm valve 21 which permits air to be sucked into the inhaler. The mouthpiece 1 has a cylindrical section and a section shaped like a truncated cone. A cyclone chamber 11 with tangential air inlet slots 12 is integrated in the cylindrical section of the mouthpiece 1. When used, the medicament 38 is flung, by the air flow sucked in through the mouthpiece, through the air duct 7 via an opening 43 onto the deflector 44. There it is disintegrated into smaller particles and then enters tangentially into the cyclone chamber 11. The secondary-air supply into the cyclone chamber 11 via the inlet slots 12 takes place via the secondary-air duct 26, visible only in the longitudinal sectional illustration of Figure 8, which is arranged in the housing flap 23 and communicates with the interior of the mouthpiece 1.

While Figure 7 shows the embodiment of the inhaler with a directly acting pressing-out device with the housing flap 23 open and a plunger 10 pressed in and no blister strip 5 inserted, the longitudinal section of Figure 8 clearly shows the position of the blister strip in the housing and the manner of functioning of the pressing-out means. In order to empty a blister cavity 31, the user exerts pressure on one of the grip plates 4 of the pressing-out plungers 10 using one finger. By means of direct force transmission, the concavely curved plunger surface 37 engages on the blister cavity 31, the covering foil 39 tears open, and the medicament 38 drops through the supply opening 20 into the duct 7, from where it can be inhaled. The torn-open covering foil remains partially connected to the remaining covering foil 39 and hangs down as a tag 8 into the supply opening. It is not illustrated in Figure 8 how the individual pressing-out plungers 10 with their grip plates 4 are mounted in the housing flap 23. On the one hand, there is the possibility of the pressing-out plungers 10 being arranged loosely in the housing flap 23 and only being held in the upper position when a blister strip 5 is inserted and their curved plunger surfaces 37 rest on the blister cavities 31. It is self-evident that the pressing-out plungers 10 must be so light that, when they are resting on the blister cavities 31, they do not damage the latter without the user exerting pressure on the grip plates 4. In order to avoid unintended loading of the blister cavities 31, the pressing-out plungers 10 can also be held in the upper position by means of engagement connections. When

pressure is exerted by the user, these engagement connections can easily be released. A further possibility is a spring mounting of the pressing-out plungers 10.

Figures 9 and 10 are cross-sectional illustrations of the inhaler according to Figures 7 and 8 with a pressing-out plunger 10 designed for asymmetrical engagement on the blister cavity. It cannot be seen in the longitudinal section of Figure 8 at what angle the edge of the curved surface 37 extends relative to the longitudinal axis of the plunger 10. If the angle is not equal to 90°, the edge always intersects a plane extending perpendicular to the longitudinal axis of the housing, i.e. to the air flow, so that the cross-section of the plunger is of asymmetrical design transversely to the longitudinal axis of the housing. Only in this way is it guaranteed that the severed covering foil, the tag 8, is aligned parallel to the air flow after the pressing-out operation and does not impede the air flow. This is to be explained again with reference to Figures 9 and 10. Figure 9 shows the inhaler with the housing flap 23 closed and a blister strip 5 inserted, the asymmetrical cross-section of the pressing-out plunger 10 being achieved in that the edge of the curved surface 37 of the plunger 10 extends at an angle not equal to 90° relative to the longitudinal axis of the plunger, and this plane of the edge intersects a perpendicular plane extending in the longitudinal direction of the housing. The curved surface 37 engages further around part of the corresponding surface of the blister cavity 31 than over the remaining part, such that the covering foil 39

is firstly torn open by the plunger 10 at a predetermined point. The blister strip 5 is pressed onto the bottom part 3 of the housing by the elastic webs 6 so that there is an airtight closure. The pressing-out plunger 10 is shaped asymmetrically in cross-section, so that the container film 33 is stretched to a greater extent on one side during the pressing-out operation (Figure 10), and the covering foil 39 tears open at this point below the more greatly loaded container film 33 and remains connected to the remaining covering foil 39 on the opposite side. The medicament 38 drops through the supply opening 20 into the air duct 7. The tag 8 of the covering foil 39 hangs down, aligned parallel to the air flow, into the supply opening 20, extending right into the air duct 7.

List of reference numerals

1 Mouthpiece
2 Single lever (upper part of the housing)
3 Bottom part of the housing
4 Grip plate of the pressing-out plunger
5 Blister strip
6 Webs for pressing the blister strip on
7 Air duct
8 Tag
9 Pressing-out lever
10 Pressing-out plunger
11 Cyclone chamber
12 Tangential air inlet slots
13 Central part of the housing
14 Pivotable bottom part of the housing
15 End piece
16 Hinge of the pressing-out levers 9
17 Hinge of the pivotable bottom part 14 of the housing
18 Receiving plate for mouthpiece 1
19 Receiving plate for end piece 15
20 Supply opening
21 Diaphragm valve
22 Recess in the housing flap 23
23 Housing flap (upper part of the housing)
24 Hinge of the housing flap 23
25 Bead along the powder duct 7
26 Secondary-air duct
27 Recess in the single lever 2
28 Notches
29 Mounting for blister strip 5

30 Recess for blister strip 5

31 Blister cavity

32 Air inlet opening

33 Container film

34 Chamber for replacement blister strips

35 Gripping grooves

36 Circular-segment-shaped recess in the upper part 2 of the housing

37 Curved plunger surface

38 Medicament

39 Covering foil

40 Inner lever arm

41 Cutout in the mouthpiece 1 and bottom part 3 of the housing

42 Pin

43 Opening to the cyclone chamber 11

44 Deflector

## PATENT CLAIMS

1. Inhaler for administering medicaments (38) from strip-shaped blister packs (5), which has a housing with a mouthpiece (1) on one side, an air inlet opening (32) on the opposite side and, between them, a duct (7) and a receiving bearing (29) for a blister strip (5) to be inserted in such a way that the covering foil of the inserted blister strip, which seals the cavities (31) containing the medicament, adjoins the duct (7), characterized in that the housing has means for pressing out the individual cavities (31) of the blister strip (5), and these means have at least one plunger (10) with a concavely curved plunger surface (37) which corresponds to the shape of the convex blister cavities (31).

2. Inhaler according to Claim 1, characterized in that the housing has at least two housing parts (2, 3, 13, 14, 23) which are pivotably connected to one another via a joint or hinges, and one of the housing parts (3, 13) has a recess (30) as a bearing for receiving the blister strip (5).

3. Inhaler according to Claims 1 and 2, characterized in that the pressing-out means (4, 10) are integrated in the upper housing part (23), and there is no lever transmission by means of which force can be transmitted to the pressing-out plunger (10) during the pressing-out operation.

4. Inhaler according to Claim 3, characterized in that the pressing-out means are four pressing-out plungers (10) which are mounted in the upper part (23) of the housing by means of grip plates (4) and, with the housing closed and a blister strip (5) inserted, can be

pressed individually downwards onto the outwardly curved cavities (31) of the blister strip (5).

5. Inhaler according to Claim 1, characterized in that the pressing-out means have a lever transmission by means of which force can be transmitted to the pressing-out plunger (10) during the pressing-out operation.

6. Inhaler according to Claim 5, characterized in that the upper part (2, 9) of the housing is designed as pressing-out means.

7. Inhaler according to Claim 6, characterized in that the pressing-out means is formed as a single lever (2) with a displaceable, engaging pressing-out plunger (10).

8. Inhaler according to Claim 6, characterized in that the pressing-out means are a plurality of levers (9), each having a pressing-out plunger (10).

9. Inhaler according to one of Claims 1 to 8, characterized in that there are inwardly directed webs (6) on the upper part (2, 23) of the housing for pressing the blister strip (5) against the receiving bearing (29) in order to fix the blister strip in the recess (30) in the closed inhaler.

10. Inhaler according to one of Claims 1 to 9, characterized in that the pressing-out means are designed in such a way that the edge of the concavely curved surface (37) of the plunger (10) engages asymmetrically on the correspondingly curved surface of the blister cavity (31).

11. Inhaler according to Claim 10, characterized in that the edge of the curved surface (37) of the pressing-out plunger (10) extends at an angle not equal to 90° relative to the longitudinal axis of the plunger

(10), and the plane of the edge intersects a perpendicular plane extending in the longitudinal direction of the housing, such that the plunger (10) engages asymmetrically on the blister cavity.

12. Inhaler according to Claim 11, characterized in that the edge of the curved surface (37) of the pressing-out plunger (10) extends at an angle of 90° relative to the longitudinal axis of the plunger (10), and the plunger (10) is connected to the housing laterally by means of a lever arm in such a way that the plunger (10), when it is pressed down by the user, carries out a movement along an arc about the pivot of the lever so that the engagement of the edge of the surface (37) on the blister cavity (31) firstly takes place on one side.

13. Inhaler according to Claim 1, characterized in that the mouthpiece (1) has, inside it, a cyclone chamber (11) with tangential air slots (12).

14. Inhaler according to Claim 1, characterized in that the air inlet opening (32) is provided with a non-return valve (21).

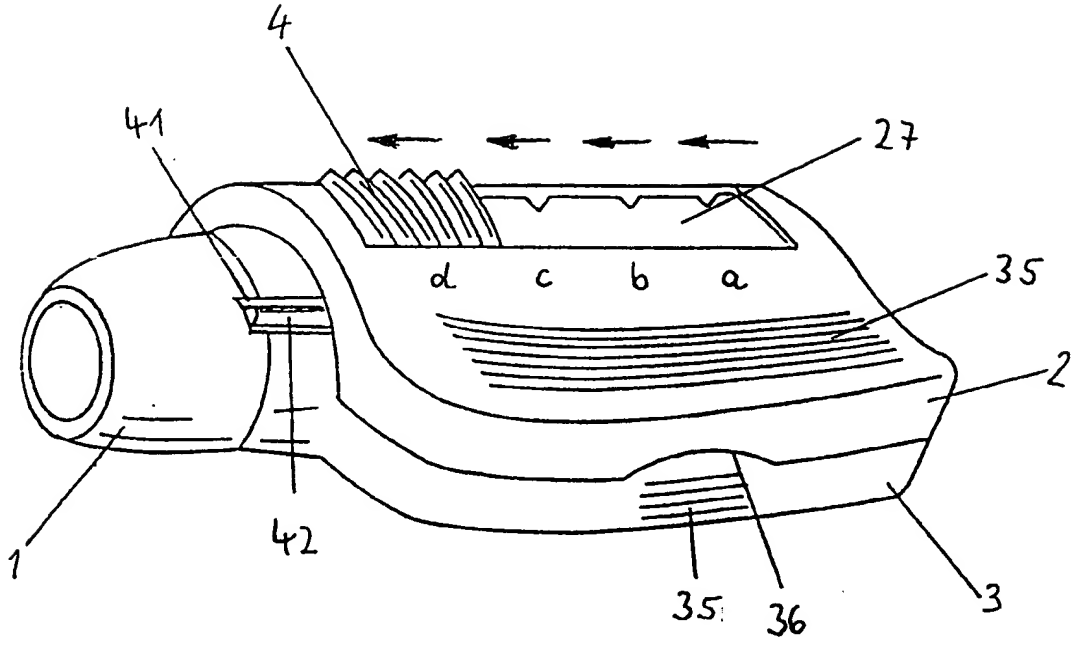


Fig.1

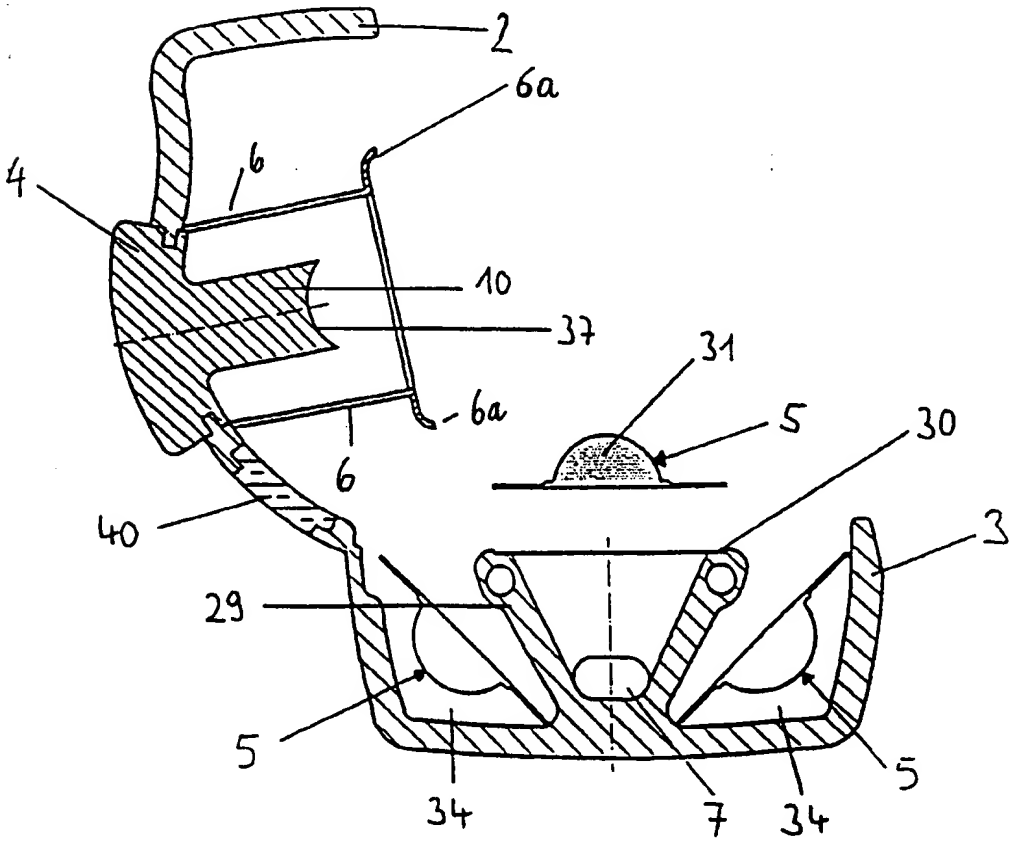


Fig.2

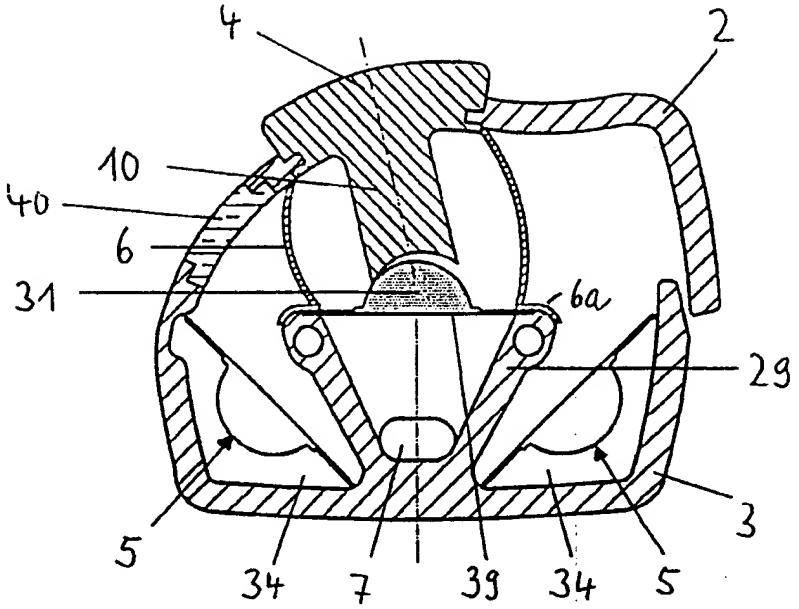


Fig.3

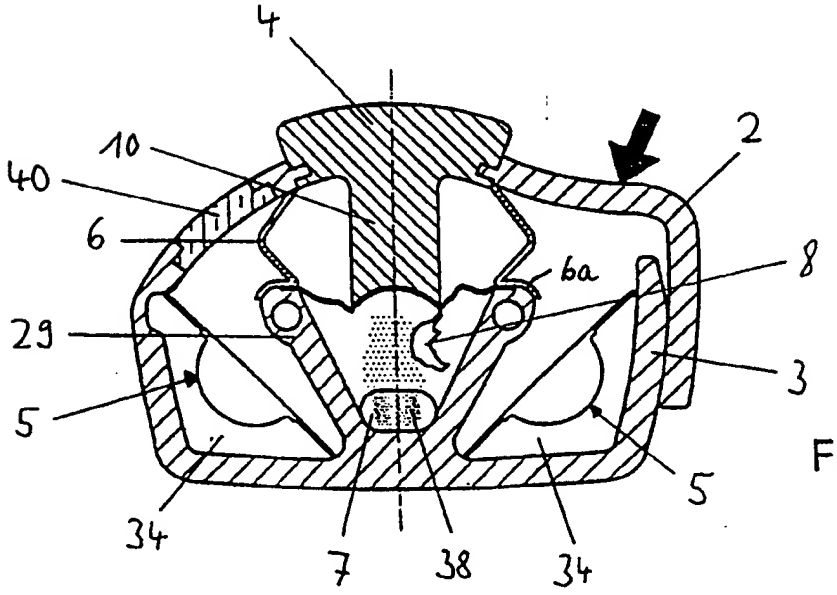


Fig.4

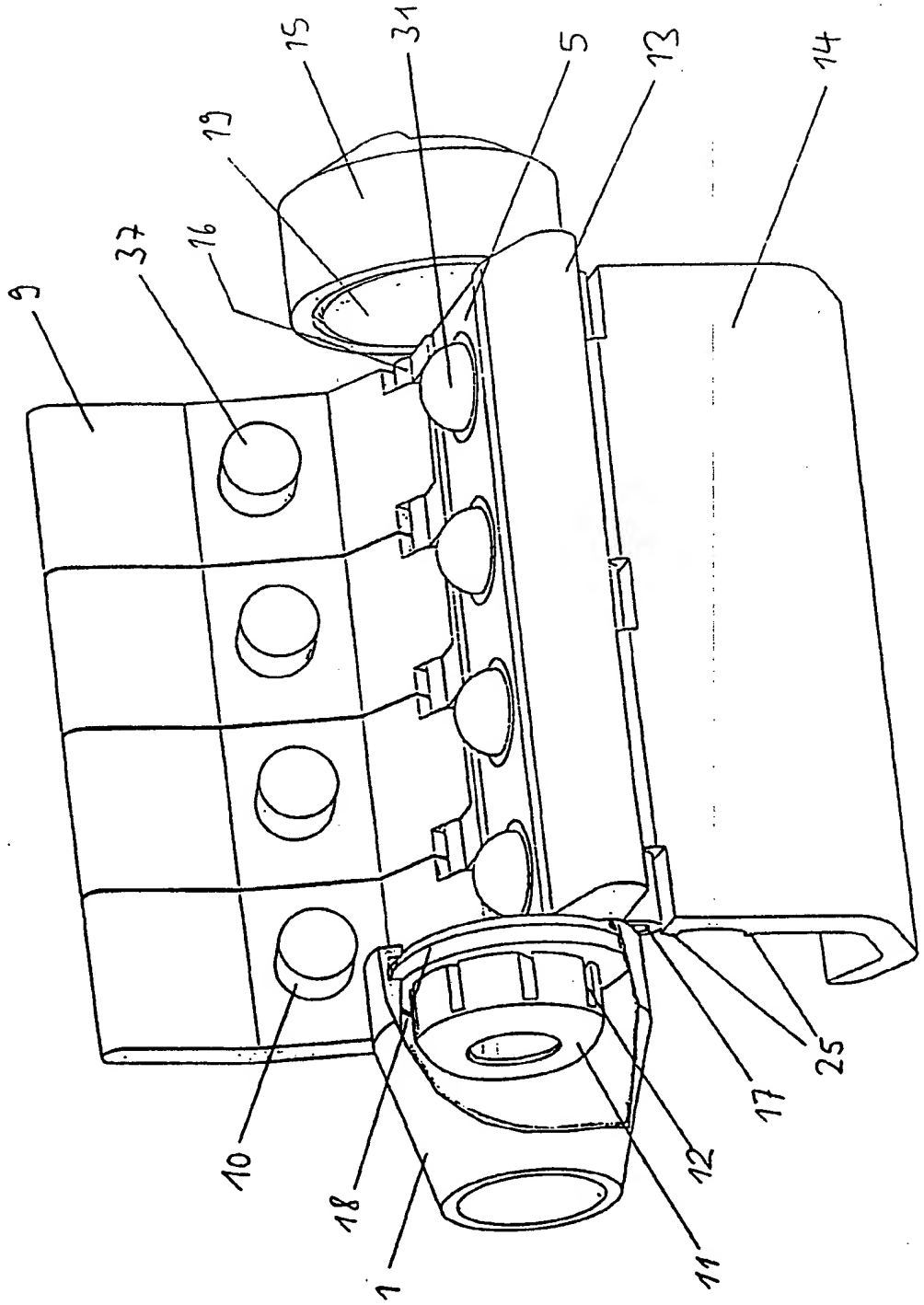


Fig.5

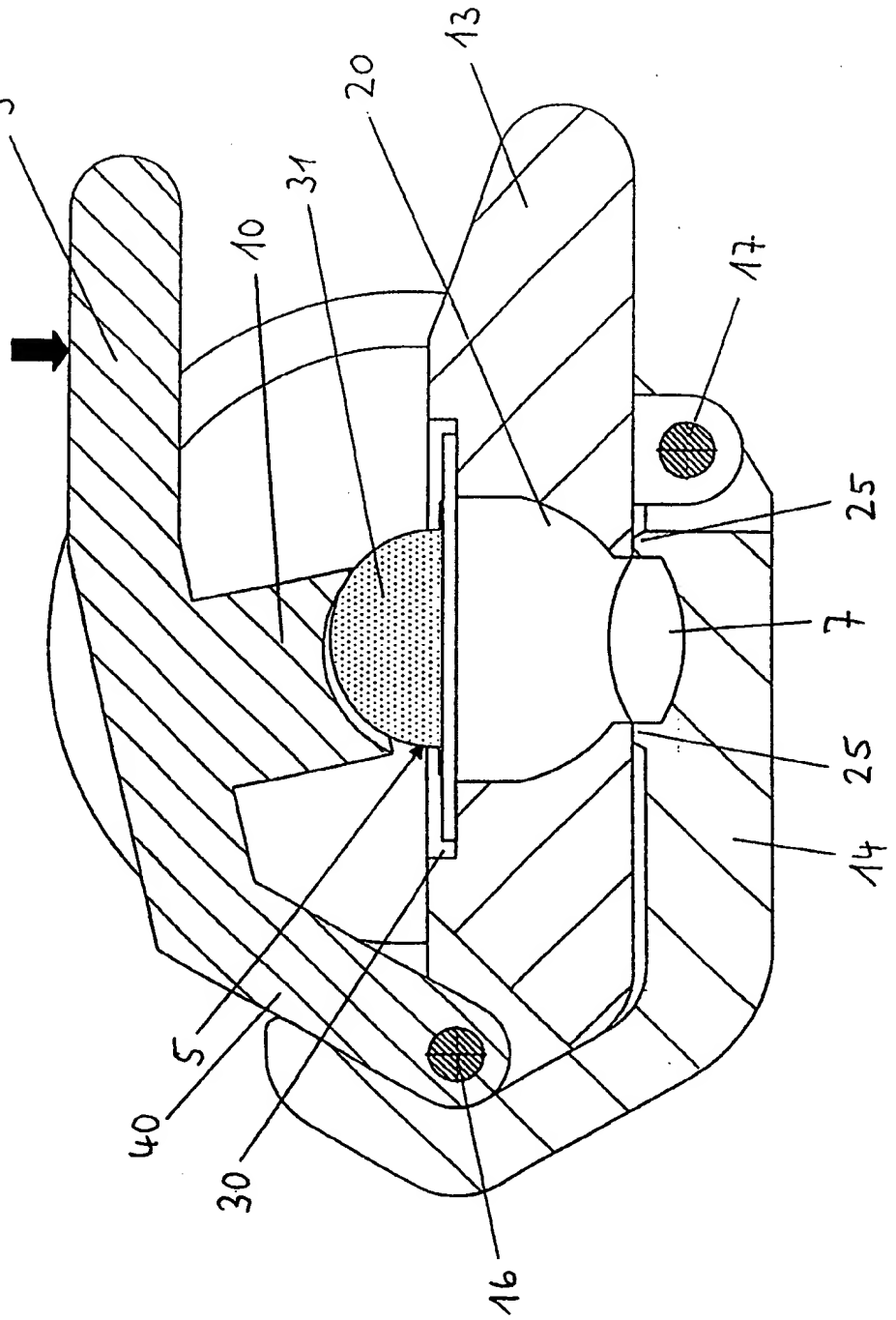


Fig.6

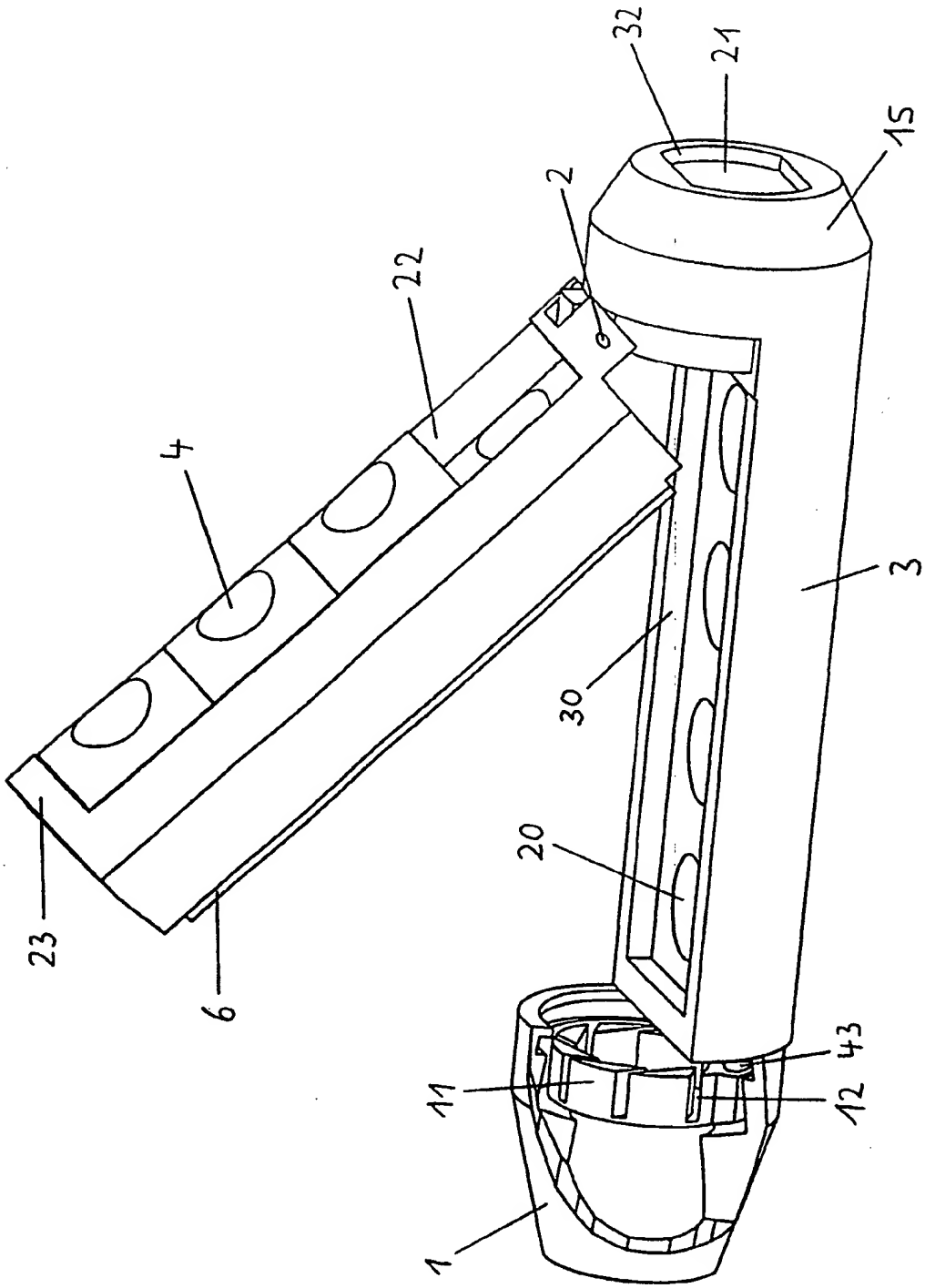


Fig.7

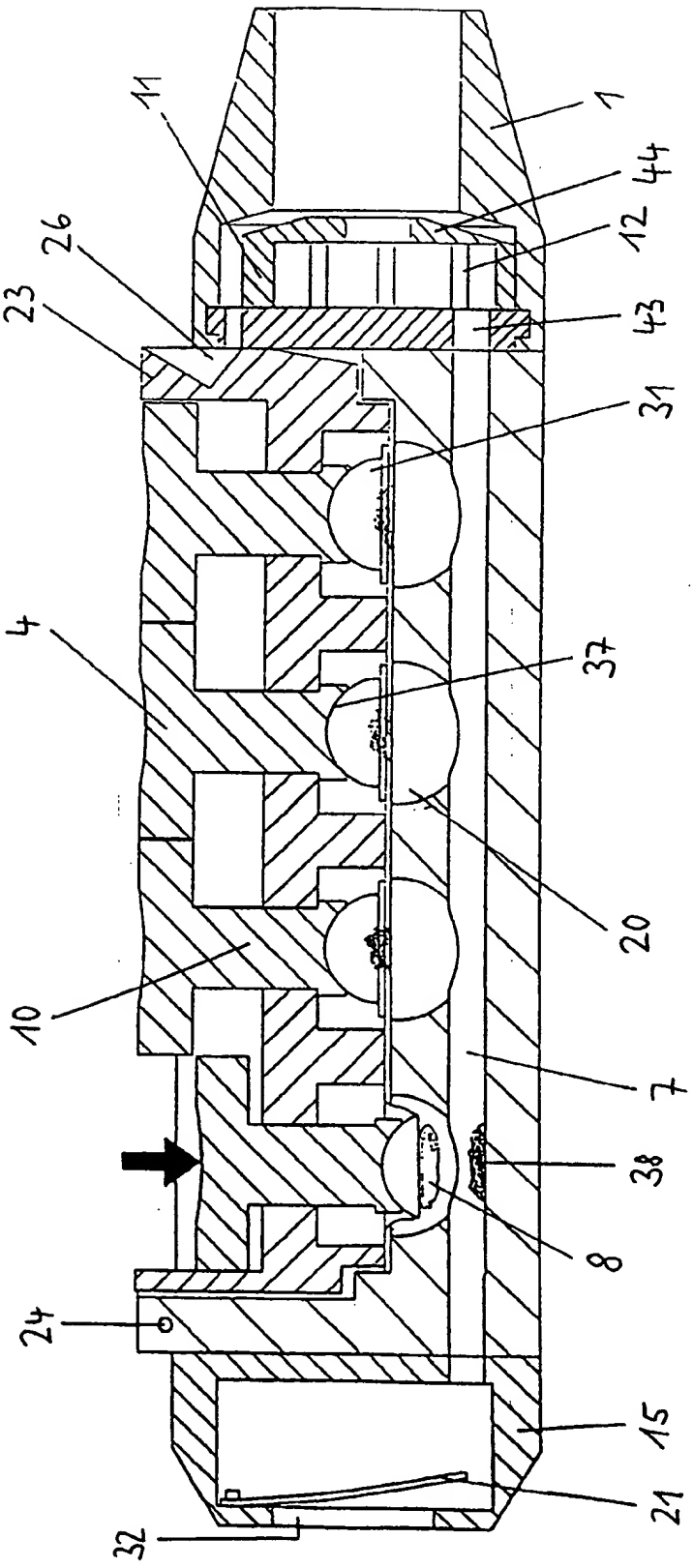


Fig.8

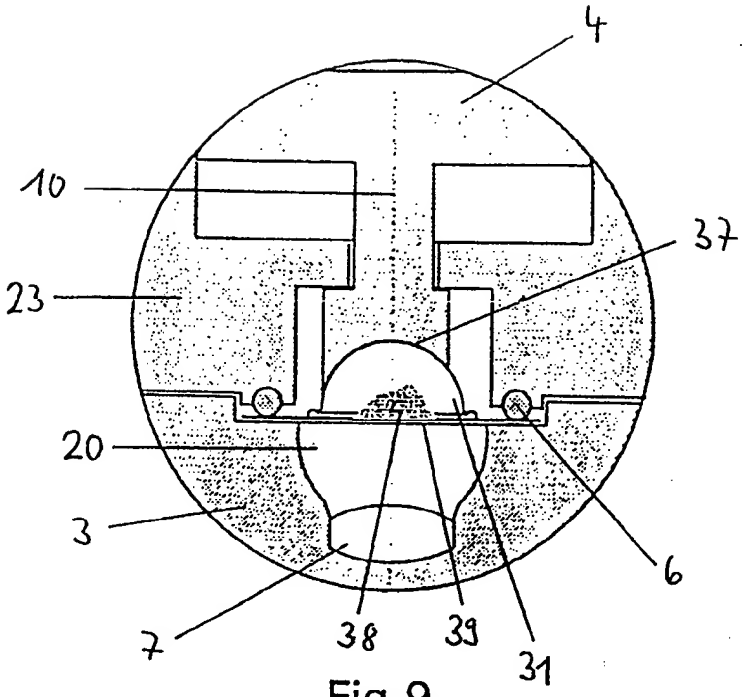


Fig.9

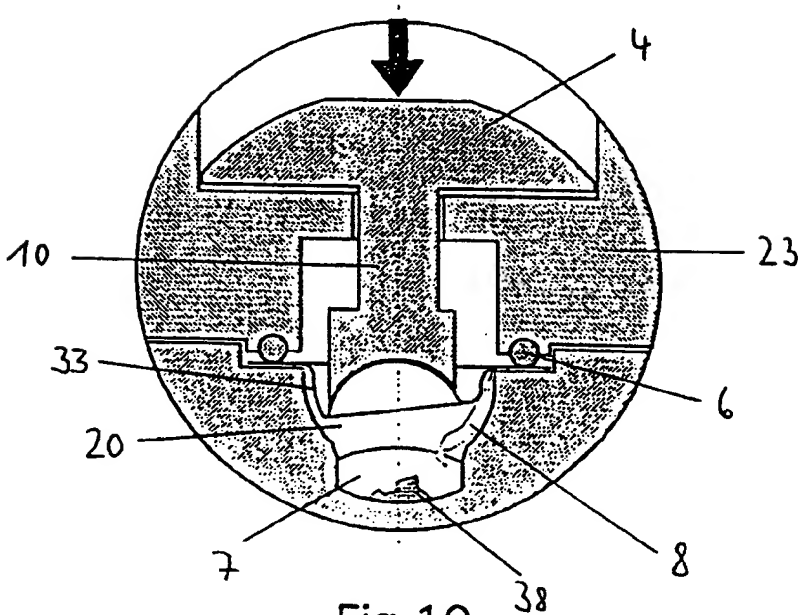


Fig.10

# INTERNATIONAL SEARCH REPORT

Inter. nal Application No
PCT/EP 96/02384

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61M15/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61M A61J B65D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X<br>Y | EP,A,0 469 814 (LILLY IND. INC.) 5 February 1992<br>see column 4, line 25 - line 30; figures 12,14 | 1,10,11<br>2,3,6,8, 9,13,14 |
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[X] Further documents are listed in the continuation of box C.

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| 30 October 1996 | 08. 11. 96 |
| Name and mailing address of the ISA<br>European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+ 31-70) 340-3016 | Authorized officer<br>Villeneuve, J-M |

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